

# Development of a synthetic pathway for a sustainable plasticizer

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*Publication date:*
2013

*Document Version*
Publisher's PDF, also known as Version of record

# Development of a synthetic pathway for a sustainable plasticizer

PhD Thesis by

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April 2013

# Preface and acknowledgements

This thesis has been submitted in the candidacy for the PhD degree from the Technical University of Denmark (DTU).

The project “Sustainable Plasticizers” has been financially supported by the Danish Advanced Technology Foundation (Højteknologifonden) and has been performed in collaboration with DuPont Nutrition Biosciences Aps (former Danisco A/S), Danish National Food institute (DTU-Food) and Department of Engineering at Aarhus University (AU).

The work reported in this thesis has been conducted at the Centre for Catalysis and Sustainable chemistry (CSC) at the Department of Chemistry at DTU (DTU Chemistry) under the supervision of Associate Professor Anders Riisager and at DuPont Nutrition Biosciences Aps under the supervision of the project manager Professor Lars Wiebe. Thank you to both for guidance in the project.

I want to give a special thanks to my co-fellow PhD-student Mathilde Grau Sørensen for good collaboration during the project and for always being there for me. Many thanks to the other co-workers in the project, especially scientist Thomas Schmidt and PhD student Seong-Chea Chua (Amanda) for help and entertainment.

Thanks to the technicians at both DTU Chemistry and DuPont Nutrition Biosciences Aps for help with analysis. Thanks to present and previous members of the CSC group.

I also want to acknowledge my friends and family for all your support.

# Abstract

The increasing concerns for using phthalates have led to the discovery of the safer alternative Grindsted® SOFT-N-SAFE (SNS) by Dansico A/S (now known as DuPont Nutrition Biosciences Aps). The main component of SNS is based on acetylated glycerol monostearate, originating from hydrogenated castor oil. SNS is a 1-1 replacement alternative to the phthalate di(2-ethylhexyl)phthalate (DEHP). This alternative is, however, too expensive to be an actual alternative to phthalates, because of the expensive starting material castor oil and the use of acetic anhydride as acetylation reagent. Besides this, the starting material is not very accessible, meaning that even if the production price of SNS was comparable to the production price of phthalates, SNS could not be produced in large enough quantities to replace the use DEHP. An alternative to SNS, the SNS-analogue (SNS-A), was suggested from glycerol monooleate originating from sunflower oil. Sunflower oil is less expensive and more accessible compared to castor oil and the SNS-A has been tested to have the same plasticizing effect and non-toxic effects as SNS. However, a sustainable and cheap way of synthesizing SNS-A has not been developed.

The aim of this project was to find an alternative, sustainable and cheap synthetic pathway for the SNS-A in collaboration with DuPont Nutrition Biosciences Aps, Danish National Food institute (DTU-Food), Department of Engineering at Aarhus University (AU) and other group members from the Centre for Catalysis and Sustainable Chemistry at Department of Chemistry at Department of Chemistry at Technical University of Denmark (DTU-Chemistry).

A three step synthetic pathway consisting of epoxidation, hydrogenation and acetylation of glycerol monooleate was early in the project suggested as the best procedure, and the different parts were divided between the parties in the project. This PhD project had three parts. The first part was to find an ionic liquid (IL) which could separate out the product from the reaction mixture and that could function as reaction media for one or more steps in the process. The

second step was developing an epoxidation procedure and the third part was developing a hydrogenation method.

The idea with using an IL as a reaction media and for product separation was also to a keep any water from the glycerol backbone of the material to avoid hydrolysis. This could be done by choosing an IL non-miscible with water, like the ones having a bis(trifluoromethylsulfonyl)amide anion. From the ILs synthesized or purchased it was not possible to find an IL which could separate out SNS. Several of the tested ILs could, however, be used as separation media after epoxidation or hydrogenation. Only one IL was miscible with the starting material and the epoxide but not the product from the hydrogenation, and all ILs where separation was possible after epoxidation step was non-miscible with the starting material. It was therefore not possible, from the ILs described here, to have a homogeneous reaction media for epoxidation with separation possible after this step.

The second part of this study, the work with developing an epoxidation procedure, can be divided into two parts. The first epoxidation method was catalytic epoxidation in ILs where product separation was possible using a heterepoly acid based catalyst and hydrogen peroxide as oxidant. The IL giving the best result was *N*-butyl-*N*-methyl imidazolium bis(trifluoromethyl-sulfonyl)amide (abbreviated [BMIm][$Tf_2N$]) and the epoxidation reaction was further investigated and optimized using this IL. Applying different reaction conditions resulted twice in a good epoxidation results, with conversions of 67 % and 70 % respectively. This, however, was not a sufficiently good result for up scaling of the process and reproducibility proved difficult. Accordingly, this method was abandoned.

The epoxidation procedure was also tested with peracetic acid with acetic acid as both solvent and by-product from the reaction. Both substrate and product are soluble in the reaction media, but as acetic acid was to be added for the final acetylation step, this did not require a solvent removal step. Already in the initial experiments this system performed very promising, and the reaction was optimized with respect to the temperature, addition time and rate of peracetic acid and substrate concentration i.e. amount of solvent. Furthermore, the effect of water concentration was also investigated. After

optimization, the result was satisfying as no large excess of peracetic acid needed to be used. The conversion rate was high at low temperatures, giving a short reaction time, and the amount of by-product low. The reproducibility of this reaction was high and it was tested many times in up to 2 L scale with the same satisfying result.

Two methods for hydrogenation of the epoxide to the mono-hydroxy compound examined, a catalytic transfer hydrogenation (CTH) using a hydrogen donor and the use of molecular hydrogen gas. CTH was conducted with selected substrates or with the epoxide of interest in this project. Several solvents, many of them ILs, were tested with three different hydrogen donors and three different catalysts, known to be efficient in CTH reactions. However, no satisfying results were obtained using CTH as a hydrogenation method.

Using molecular hydrogen gas for hydrogenation also resulted in problems. The hydrogenation of the epoxide obtained from epoxidation with peracetic acid gave mainly the saturated monoglyceride instead of the mono-hydroxy compound as intended. Several heterogeneous metal catalysts and reaction conditions were tested, but it was not possible to find a suitable method for the hydrogenation.

Overall, this PhD study has established a potentially industrially viable epoxidation protocol as part of a new reaction pathway for the synthesis of SNS-A.

# Resumé

En stigende bekymring ved anvendelsen af ftalater har ført til opdagelsen af det mere sikre alternativ Grindsted® SOFT-N-SAFE (SNS) af Danisco A/S (nu kendt som DuPont Nutrition Biosciences Aps). Hovedbestanddelen af SNS er baseret på acetyleret glycerol(12-hydroxy)monostearat, som kommer fra hydrogeneret ricinusolie. SNS er et 1:1 alternativ til blødgøreren di(2-ethylhexyl)ftalat (DEHP). Dette alternativ er dog for dyrt til at kunne være et reelt alternativ til de blødgørende ftalater pga. udgangsstoffet ricinusolie og eddikesyreanhydrid, som anvendes som acetyleringsreagens. Herudover er ricinusolien ikke let tilgængeligt, hvilket betyder at selvom produktionsprisen for SNS ville være sammenlignelig med produktionsprisen for ftalater, ville SNS ikke kunne produceres i stor nok mængde til at kunne erstatte DEHP. Der er derfor blevet foreslået endnu et alternativ, en SNS-analog (SNS-A), som syntetiseres ud fra glycerolmonooleat, som kommer fra solsikkeolie. Solsikkeolie er både billigere og lettere tilgængelig end ricinusolie og SNS-A er blevet testet til at have den samme blødgørende effekt og er lige så uskadelig som SNS. Der er dog ikke blevet fundet en bæredygtig og billig metode til at syntetisere SNS-A.

Målet med dette projekt var derfor at finde en alternativ syntesemetode, som var både billig og bæredygtig. Projektet blev lavet i samarbejde mellem DuPont Nutrition Biosciences Aps, Fødevareinstituttet ved Danmarks Tekniske Universitet (DTU-Food), Institut for Ingeniørvidenskab ved Aarhus Universitet (AU) og andre medlemmer fra Center for Katalyse og Bæredygtig Kemi ved Danmarks Tekniske Universitet (DTU-Kemi).

Tidligt i projektforløbet blev en tre-trins syntese foreslået som den realistiske metode. Denne bestod af epoxidering, brintning og acetylering af glycerol monooleat, og de forskellige delprojekter blev fordelt på de forskellige grupper i projektet. Dette ph.d. projekt indeholdte tre dele. Første del gik ud på at finde en ionisk væske (IL), hvorfra produktet kunne separeres fra

reaktionsblandingen og som kunne fungere som reaktionsmedie for en eller flere trin i processen. Anden del gik ud på at udvikle en epoxideringsprocedure og tredje del gik ud på at udvikle en brintningsmetode.

Idéen med at anvende ILs som solvent, både til reaktionen og til faseadskillelse af produktet var også at holde vand væk fra den hydrolyserbare estergruppering i monoglyceridet. Dette kunne gøres ved at vælge en IL som ikke var blandbar med vand, såsom en IL med en bistriflimid anion. Flere ILs blev syntetiseret eller købt, men ingen af dem kunne faseadskille med SNS. Flere af de testede ILs kunne dog anvendes til at faseseparere efter epoxidering eller brintning. Kun en IL var blandbar med startmaterialet og epoxidet, men ikke med produktet efter brintningen, og alle ILs hvor faseadskillelse var mulig efter epoxidering, var desværre ikke-blandbare med startmaterialet. Ud fra de ILs beskrevet i dette projekt har det derfor ikke været muligt at finde en IL, hvor det var muligt med homogene reaktionsbetingelser under epoxideringen, men med produkt-faseadskillelse efter reaktionen.

Anden del af dette projekt var at udvikle en epoxideringsprocedure. Dette kan deles i to dele, første del var en katalytisk epoxidering, som blev testet i de ILs hvor faseadskillelse var mulig. Metoden bestod af en heteropolysyre-baseret katalysator og brintoverilte som epoxideringsreagens. Den IL der gav det bedste resultat var *N*-butyl-*N*-methylimidazolium bis(trifluoromethyl-sulfonyl)amid (forkortes [BMIm][$Tf_2N$]) for epoxideringsreaktionen blev undersøgt og optimeret med denne IL. Ved at anvende forskellige reaktionsbetingelser blev der to gange opnået et godt epoxideringsresultat, med omdannelser på henholdsvis 67 % og 70 %. Dette var dog stadig ikke tilfredsstillende for en opskaling af reaktionen, og da det derudover var svært at reproducere de gode resultater, blev denne metode fravalgt.

Epoxideringsreaktionen blev også testet med pereddikesyre, med eddikesyre som solvent og biprodukt fra reaktionen. Både substrat og produkt er opløselige i reaktionsblandingen, men da eddikesyre alligevel skulle tilsættes som acetyleringsreagens i sidste trin, gav dette ikke de store betænkeligheder. Allerede i de tidlige forsøg virkede systemet meget lovende og systemet blev derfor optimeret med hensyn til reaktionstemperatur, mængden og

hastigheden af pereddikesyretilsætningen samt substrat koncentrationen, dvs. hvor meget solvent der skulle anvendes. Desuden blev effekten af vand koncentrationen i systemet også undersøgt. Efter optimering blev et tilfredsstillende resultat opnået hvor der ikke skulle bruges stort overskud af pereddikesyre, hvor omdannelsen til epoxid var høj, temperaturen lav, reaktionstiden kort og mængden af uønskede sidereaktioner lav, samt at det var nemt at reproducere resultaterne. Reaktionen blev testet flere gange i 2 L med det samme tilfredsstillende resultat.

To forskellige metoder til brintingen af epoxidet til mono-hydroxy forbindelsen blev testet ved hjælp af katalytisk transfer hydrogenering (CTH), hvor der anvendes en hydrogendonor, eller ved den mere traditionelle hydrogenering med brint gas. CTH blev testet med flere modelforbindelser eller med epoxidet fra projektet. Forskellige solventer, herunder flere ILs, blev testet sammen med tre forskellige hydrogendonorer og tre forskellige katalysatorer, som er kendt for at være gode ved CTH reaktioner. Der blev dog ikke opnået et tilfredsstillende resultat med denne metode.

Anvendelse af brint til hydrogeneringen resulterede også i problemer, da brinting af epoxidet fra pereddikesyre-processen resulterede primært i mættet monoglycerid fremfor den ønskede mono-hydroxy forbindelse, som dannes ved reduktiv åbning af epoxidringen. Flere forskellige heterogene metal katalysatorer og reaktionsbetingelser blev testet, men det var ikke muligt at finde en passende brintningsmetode som undertrykkede dannelsen af biproduktet.

Samlet set gav dette ph.d. projekt en potentiel industriel epoxideringsmetode som en del af en ny reaktionsvej til produktionen af SNS-A.

# Abbreviations

| | |
|---|---|
| $[BMIm]^+$ | *N*-butyl-*N*-methylimidazolium |
| CTH | Catalytic transfer hydrogenation |
| DAGMO | Diacetyl glycerol monooleate |
| DBP | Dibutyl phthalate |
| DEHP | Di(2-ethylhexyl)phthalate (also known as DOP) |
| DHGMS | 9,10-dihydroxy glycerol monostearate (2,3-dihydroxypropyl 9,10-dihydroxyoctadecanoate) |
| DIDP | Diisodecyl phthalate |
| DINP | Diisononyl phthalate |
| DOP | Dioctyl phthalate (also known as DEHP) |
| EDAGMS | 9,10-epoxy diacetyl glycerol monooleate (3-((8-(3-octyloxiran-2-yl)octanoyl)oxy)propane-1,2-diyl diacetate) |
| EGMS | 9,10-epoxy glycerol monostearate (2,3-dihydroxypropyl 8-(3-octyloxiran-2-yl)octanoate) |
| Eq | Equivalent(s) |
| GMO | Glycerol monooleate |
| GMS | Glycerol monostearate |
| HPA | Heteropoly acid |
| IL | Ionic liquid |

| | |
|---|---|
| MBT | Monobutyl phthalate |
| MEHP | Mono-2-ethylhexyl phthalate |
| MHGMS | Monohydroxy glycerol monostearate (2,3-dihydroxypropyl 9-hydroxyoctadecanoate or (2,3-dihydroxypropyl 10-hydroxyoctadecanoate)) |
| MOA | methyl oleate |
| MSTFA | *N*-Methyl-*N*-trimethylsilyl-trifluoroacetamide |
| Mt | Million tons |
| NOAEL | The no-observed-adverse-effect-level |
| PE | Polyethylene |
| PET | Polyethylene terephthalate |
| PP | Polypropylene |
| PS | Polystyrene |
| PUR | Polyurethane |
| PVC | Polyvinylchloride |
| RT | Room temperature |
| RTIL | Room temperature Ionic liquid |
| SNS | Grindsted® SOFT-N-SAFE |
| SNS-A | SOFT-N-SAFE-analogue |
| TEAB | Tetraethylammonium bromide |
| TEAI | Tetraethylammonium iodide |
| $[Tf_2N]^-$ | Bis(trifluoromethylsulfonyl)amide |
| TMCS | Trimethylchlorosilane |

# Publications

The following is a list of presentations at international conferences and peer review publications as part of the PhD study.

## Posters at conferences and summer schools

Mathilde Grau Sørensen, Helle Søndergaard, Anders Theilgaard Madsen, Anders Riisager. Application of Ionic Liquids in Production of Fuel and Chemicals from Bio-Oil (EUCHEM Conference on Molten Salts and Ionic Liquids, Bamberg, Germany, March 14th-19th **2010**)

Helle Søndergaard, Anders Riisager. Ionic Liquids as Reaction Media for Transfer Hydrogenation of Epoxides (Gordon Research conference on Green Chemistry, Davidson, USA, July 25th-30th **2010**)

Helle Søndergaard, Anders Theilgaard Madsen, Anders Riisager. Application of Ionic Liquids Catalysts in the Production of Biodiesel (14th Nordic Symposium on Catalysis, Helsingør, Danmark, August 29th-31st **2010**)

Helle Søndergaard, Anders Riisager. Ionic Liquids Catalysts for Biodiesel Synthesis (OChem Graduate School at Aarhus University, PhD autumn school: Green Organic Chemistry, Sandbjerg, Denmark, October 28th-30th **2010**)

Helle Søndergaard, Anders Riisager. Ionic Liquids as Catalysts and Solvents (DTU Chemistry PhD Seminar, Gentofte, Denmark, November 4th-5th **2010**)

Helle Søndergaard, Anders Riisager. Catalytic Transfer Hydrogenation of Epoxides Performed in Ionic Liquids (15th annual Green Conference & Engineering Conference, Washington, USA, June 15th-18th **2011**)

Helle Søndergaard, Anders Riisager. Functionalized Ionic Liquids: Synthesis, Characterization and Application (4th international congress on ionic liquids (COIL-4), Arlington, USA, June 20th-23rd **2011**)

Helle Søndergaard, Mathilde Grau Sørensen, Anders Riisager. Ionic Liquids as Reaction Media with Phase Separation Properties: Cation Effect (5th Workshop on Fats and Oils as Renewable Feedstock for the Chemical Industry, Karlsruhe, Germany, March 18th-20th **2012**)

## Peer Reviewed Publications

Madsen, A.T., Søndergaard, H., Fehrmann, R., Riisager, A., Challenges and Perspectives in the Production of Diesel from Biomass, *Biofuels* 2 (**2011**) 465–483

# Index

# Chapter 1
# Motivation for the project

Plasticizers are added to materials to increase the fluidity. In the plastic polyvinyl chloride (PVC) the plasticizers mostly used are phthalates.[1] But phthalates are suspected to be endocrine disruptors[2] and alternatives are therefore wanted. Danisco A/S (now known as DuPont Nutrition Biosciences Aps) has developed a sustainable alternative to phthalates, and without the endocrine disrupting effect.[3] This product is known as Grindsted® SOFT-N-SAFE (SNS) and is made from hydrogenated castor oil. The major concern about SNS is the price, as this alternative is 3-4 as expensive as the phthalate.[4,5] Danisco A/S has been looking for alternatives to the starting material and process. The product, SNS-analogue (SNS-A) is made from the much cheaper sunflower oil, and has shown same good results as SNS.[6] This project aims at developing a process for preparation of SNS-A and is conducted in collaboration with DuPont Nutrition Biosciences Aps, Danish National Food institute (DTU-Food), Department of Engineering at Aarhus University (AU) and Department of Chemistry at the Technical University of Denmark (DTU-Chemistry).

## 1.1 Plastics and plasticizers

Plastics are an essential part of everyday life for all of us. It is in the houses we live in, in the cars we drive in, in the toys, computers and televisions that we all enjoy. Go to the supermarket and a lot of food you put into your basket is wrapped in plastics. The word plastic is derived from the Greek words *plastos* (meaning molded) and *plastikos* (meaning fit for molding), which refers to the materials ability to be formed into many different shapes.[7]

The production of plastics has been increasing with approximately 9 % per year during the last 60 years, although with a small decreases with e.g. the economic crisis in 2008/2009. In 2011 the amount of plastics produced in the world was around 280 million tons (Mt).[8] In Europe most of the plastics were used in packaging (39.4 %) and building and construction (20.5 %). There are six major types of plastics. These are polyethylene (PE), polypropylene (PP), PVC, polystyrene (PS), polyethylene terephthalate (PET) and polyurethane (PUR). These six types of plastics accounted for around 80 % of all plastics used in 2011 in Europe. PE accounted for 29 % and was mainly used in packaging. PP accounted for 19 % and was also used a lot in packaging. The third mostly used plastic type was PVC with 11 %, which was mainly used in building and construction.[8]

Plasticizers are materials that are incorporated into the plastic polymer to increase the flexibility and workability. This can for instance be done by lowering the glass transition temperature $T_g$, thereby increasing the flexibility of the material.[9] The plasticizer can also be generated *in situ* by cleaving of the polymer to smaller parts.[10] In 2003, the world market for plasticizers was more than 4.6 Mt and 90 % of this was produced for PVC. For Europe alone, the amount is about 1.3 Mt.[9] When plasticizing e.g. PVC a large amount of plasticizers are needed and migration of the plasticizer is therefore of great concerns.[3,11,12]

There are two ways a plasticizer can perform. If the polymer is chemically combined with the plasticizer, the plasticizer is known as an internal plasticizer. But if the polymer is not changed chemically by the plasticizer, it is known as an external plasticizer.[1,10] Plasticizers can also be divided into two other groups: primary and secondary. Primary plasticizers are plasticizers that actually increase the flexibility of the polymer it is added to. Secondary plasticizers on the other hand do not themselves make the polymer softer, but enhances the effect of primary plasticizers. Secondary plasticizers can therefore not be used on their own.[1]

## 1.2 Phthalates

Phthalates are *ortho* esters of phthalic acid as shown in Figure 1-1. Phthalates are synthesized by an esterification between two molecules of an alcohol and phthalic acid. The alcohols can be two different ($R_1 \neq R_2$) or the same ($R_1 = R_2$). Many different alcohols can be used, but in general if the alcohol is shorter than $C_4$ the phthalate is too volatile to use a plasticizer whereas if it is larger than $C_{13}$ the phthalate has limited compatibility towards the plastic polymer. Often the alcohol is therefore an alkyl chain with the length $C_4$-$C_{13}$.[9]

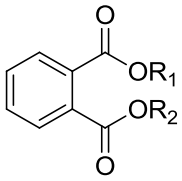



**Figure 1-1: General structure of phthalates. $R_1$ and $R_2$ can either be the same or two different.**

The application of phthalates as plasticizers goes back to 1920[11] and today phthalates are the most used plasticizer.[13] In 1999 92 % of all plasticizers were of the phthalate type. The most widely used phthalate is di(2-ethylhexyl)phthalate (DEHP) (51 %), diisodecyl phthalate (DIDP) (21%) and diisononyl phthalate (DINP) (11 %).[14] DEHP is sometimes referred to as dioctyl phthalate (DOP). DEHP was introduced to the marked in 1930 and have ever since been the most used phthalate.[11]

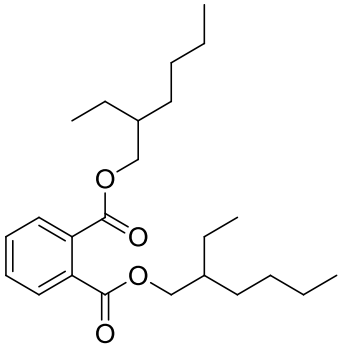



**Figure 1-2: Chemical structure of di(2-ethylhexyl)phthalate (DEHP)**

Animal studies have shown that DEHP has a negative effect on male reproduction by having a negative effect on the testes.[2] The negative testicular effect is seen by a decrease of size and a changed histology of the organ.[15] The effect is caused by an increase in the testosterone level in the testes and a decrease in the testosterone level in the plasma.[16] This leads to malformation of the testosterone-dependent tissues e.g. the testes.[17] It is believed that this changed level of testosterone can be linked to a low concentration of zinc in the testes.[18] By administrating DEHP or dibutyl phthalate (DBP) to pregnant or lactating rats, the male offspring will be less masculine and more feminine. This can for instance be seen by a decrease in the anogenital distance (the distance from anus to the genitals).[17] Administrating the phthalate during puberty has also a negative effect.

Migration of phthalates from lactating women or from food packaging[19] and medical devices[20] has been observed. It is therefore important to know if phthalates have a negative effect on humans. Endocrine effects of phthalates on humans have been investigated, although most knowledge about phthalates is still from animal studies. It can be difficult to extrapolate the knowledge from animals studies to humans, and it is therefore important to have human test objectives as well.[21] Most work with humans and phthalates has been on DBP and its metabolite monobutyl phthalate (MBT), but also DEHP and its metabolite mono-2-ethylhexyl phthalate (MEHP). Exposure to some phthalates indicates a change in the reproductive hormones of adult men and low sperm concentration.[20,22–24] Other investigation have however not observed the same effect, although they agree on a hazardous effect of phthalates.[25] It has also been shown that the metabolites of phthalates have a DNA damaging effect of the sperm cells.[26] The prenatal effect of phthalates on the anogenital distance has also been investigated in humans. It was found that if the mother showed elevated levels of phthalates during pregnancy, the boys would have shorter anogenetial distance and a testicular descent.[27] According to Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR) in 2008 there is no conclusive evidence that DEHP from medical applications has a harmful effect on humans.[28] Further investigations must be conducted before a final conclusion can be made on the endocrine effect of phthalates in humans.[21]

The negative endocrine effect of DEHP and other phthalates have led to the restriction of uses of different pthtalates.[29] Six phthalates have been banned in plastics where children might be exposed in EU in 2005 and in USA in 2008.[30] Although banned in EU and USA, other parts of the world such as China and India continue the use of these phthalates in children's toys.[31]

## 1.3 Developing new alternatives

There are nine major challenges to look at regarding developing plasticizers:[11]

- Migration out of plastic: The migration of the plasticizer from the plastic into the surroundings is determined by the solubility of the plasticizer (the compatibility) and the diffusion coefficient (the mobility).[32] When the plasticizer migrates out of the polymer, the polymer's flexibility is no longer retained. Furthermore, the plasticizer can have a bad effect on the surroundings, both looking at health and environment.[11]
- High temperature flexibility: Because of the often low boiling point of plasticizers and a high vapor pressure, plasticizers are often degraded rapidly at high temperatures. Phthalates have shown to suppress some of the degradation process of PVC, the dehydrochlorination, and hence when phthalates evaporate, the PVC degrades faster.
- Low temperature lubricity: Most plasticizers do not work well at low temperatures. This could be due to high melting points of the plasticizers, making the plasticizers solid at low temperatures. In this way, the plasticizer is a solid before the polymer reaches its $T_g$ and the effect of the plasticizer is therefore very small.
- Health and environmental effects: Migration or evaporation of the plasticizer is the main route of exposure for humans to the plasticizer. Especially phthalates have been of great concern here because of the proposed negative endocrine effect.
- Flammability concerns: Many plasticizers increase the flammability of the plastics because they themselves are more flammable. Phthalates are known to increase the smoke production, ease of ignition and burning rate of PVC.

- Compatibility with new polymers: Because new polymers are developed all the time it is important to find new plasticizers that are compatible with these polymers.
- Stability to ultraviolet rays: The degradation of the polymers by ultraviolet rays may decrease the plasticizers efficiency.
- Biodegrability: For polymers with biomedical applications, or applications where the product will end up in nature, it is a good idea to have both the polymer and the plasticizer to be biodegradable. For these materials there are more stringent requirements as they are released into the environment, especially looking at health and safety issues.
- Improved material lifetime: If the lifetime of the plasticizer is improved, so is the lifetime of the polymer it is added to, hereby reducing the costs of the polymeric material.[11]

Development of new plasticizers often involves looking at several of the above mentioned problems.

## 1.4 Alternatives to phthalates

Health issues and the following restriction on different phthalates have led to findings of alternatives. Already in 1999 a decrease in the demand for DEHP was observed, because of the ongoing debate about phthalates.[33]

One alternative is Hexamoll® DINCH, developed by the German chemical company BASF and launched in 2002. It is used in PVC, where it can substitute phthalates without major changes in the production. Hexamoll® DINCH has a stronger association to PVC and migration is thereby reduced.[34] Hexamoll® DINCH has gone through thoroughly toxicological testing with good results.[35–37] It has been seen in medical application and in 2006 it was also recommended for food contact applications.[33,35,37] Hexamoll® DINCH has the chemical name di-isononylcyclohexane (see Figure 1-3).[38] It is produced by hydrogenation of the aromatic ring in DINP and offers an improved temperature performance compared to it.[33]

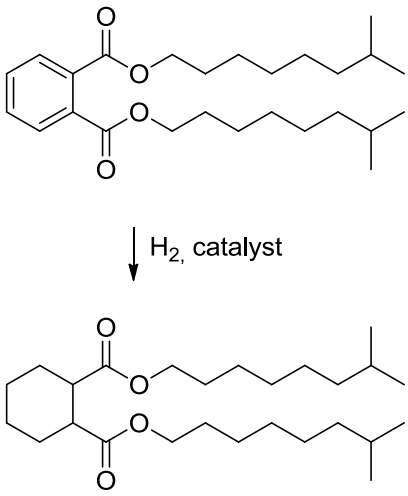



**Figure 1-3: Synthesis and chemical structure of Hexamoll® DINCH, a sustainable alternative to phthalates, developed by BASF.**

Palatinol® N is a trade name of DINP at BASF[39] and is the starting material for Hexamoll® DINCH. Hexamoll® DINCH is produced by a catalytic hydrogenation Palatinol® N.[40,41]

Citrates are also important as alternatives. Although not new to the marked, they are still important because of low toxicity and new citrates are still developed. One example is Uniplex 84, developed by Unitex Chemical Corporation. The chemical name for Uniplex 84 is acetyl tributyl citrate (see Figure 1-4).[28,42] It was approved in USA[43] and EU[33] for the use in food packaging and PVC toys. It has been tested very thoroughly and has very low toxicity.[28]

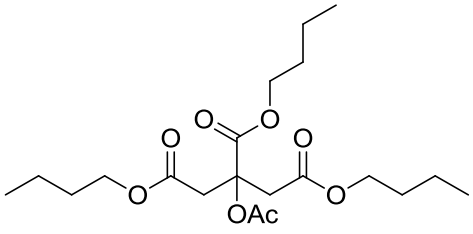



**Figure 1-4: Chemical structure of Uniplex 84, a newly developed citrate as alternative to phthalates. Developed by Unitex Chemical Coporation**

An alternative to phthalates is terephthalates or esters of terephthalic acid or *para* substituted isomers of phthalic acid. None of the negative health and environmentally issues have been observed with terephthalates. Eastman Chemical Company has launched Eastman 168™ as an alternative to phthalates in plastisols.[44] As seen in Figure 1-5 the structure is much like DEHP, only with *para* substitution instead of *ortho*. Good properties as low temperature flexibility and almost no migration are worth mentioning. It does not have the negative endocrine effect as DEHP.[33]

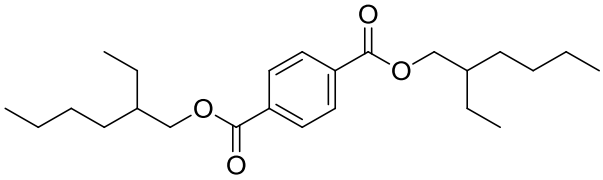


**Figure 1-5: Chemical structure of Eastman 168™, developed by Eastman Chemical Company as an alternative to phthalates.**

The German company Lanxess Energizing Chemistry has launched the phthalate alternative Mesamoll® II. This consists of alkylsulphonic acids phenyl esters, with the alkyl chain being from $C_{10}$ to $C_{21}$.[45] It has been approved for the use in PVC in food contacts.[46] Different phosphates like di- or tri(2-ethylhexyl) phosphate can also be used as a plasticizer in PUR and PVC.[31]

Adiapates are esters of a linear $C_6$-dicarboxylic acid. The most common one is di(2-ethylhexyl) adipate (see Figure 1-6), which is used in food packaging.[47] It has CAS registry number 103-23-1. This is not a newly developed plasticizer, but is very important because of the structural resemblance to DEHP. This is the plasticizer mostly used in food packaging PVC film and it shows no signs of genotoxicity or carcinogenicity.[48,49] It is also used in PVC toys.[31] It is sold under the trade name OXOSOFT DOA by the fairly new company OXEA (founded in 2007).[50]

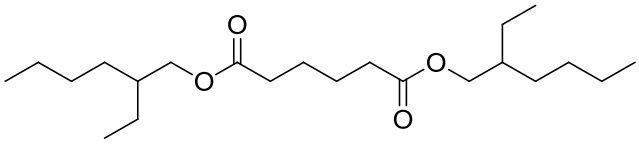


**Figure 1-6: Chemical structure of di(2-ethylhexyl) adiapate, not a new alternative to phthalates, but still a good alternative.**

Epoxidized soybean oil is another not new alternative.[31,51] It is also known as epoxidized trilinolein (see Figure 1-7). This plasticizer can decrease the ultraviolet degradation of PVC and it is used in the sealing closures of glass jars of sterilized food like baby food. Because of a high content of plasticizer in this sealing, migration can be a problem, and it is therefore important that the plasticizer does not have any negative health issues.[51] The high molecular weight of epoxidized soybean oil however decreases the migration and it is made from renewable resources. It improves low temperature properties of PVC and is sold under the trade name Vikoflex® 7170 by Arkema.[52]

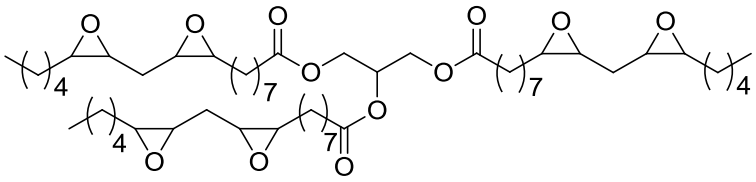


**Figure 1-7: Chemical structure of epoxidized soybean oil.**

Another alternative is tri(2-ethylhexyl) trimellitate (see Figure 1-8). Its plasticizing effect can be compared to phthalates.[31,53] The higher molecular weight and thereby lower vapor pressure compared to phthalates gives a decreased migration. It is mainly used in medicinal applications.[53] The plasticizer shows good properties at high temperatures. OXSOFT TOTM is a trade name for tri-2-ethylhexyl trimellitate by the fairly new company OXEA.[50]

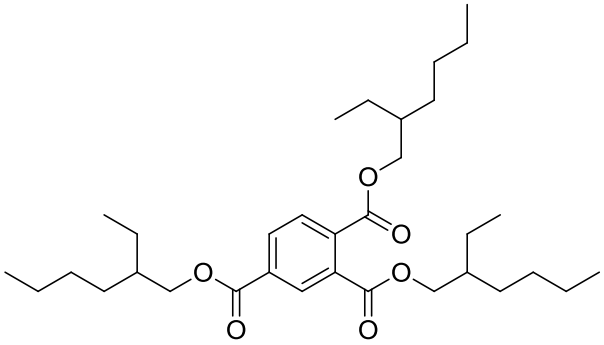


**Figure 1-8: Chemical structure of tri-2-ethylhexyl trimetallitate, an alternative to phthalates.**

## 1.5 Grindsted® SOFT-N-SAFE (SNS)

In 2005 SNS was released as an alternative to phthalates,[54] but the discovery of the plasticizer potential of SNS was made already in 1998.[55] SNS is a one-to-one replacement to DEHP and can replace phthalates without major changes in the production of plastics.[12,28,56–58] Some application areas are food contact PVC, plastisol formulations or PVC based medical devices.[3,12,56] It is by far one of the safest alternatives to phthalates and is also considered a better alternative compared to epoxidized soybean oil and di(2-ethylhexyl) adipate. The molecular weight of SNS is higher than that of DEHP, giving low volatility, but this does not compromise the plasticizing efficiency. The molecular weight is comparable to tri(2-ethylhexyl) trimellitate but the volatility is higher. This, however, is not a problem as a lower loading of SNS is needed, reducing the total volatility.[12]

The main component of SNS is fully acetylated 12-acetoxy glycerol monostearate (fully acetylated 12-acetoxy GMS) as showed in Figure 1-9. This represents 85 % of SNS. Around 10 % of SNS is acetylated glycerol monostearate (acetylated GMS). It is odorless and colorless.

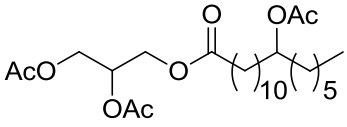


**Figure 1-9: The chemical structure of SNS: fully acetylated 12-acetoxy glycerol monostearate.**

As SNS is made from a vegetable oil, it is fully biodegradable and metabolizes like any other vegetable oil and is therefore fully digestible.[12,55] It is tested to have the same quality, durability and plasticizing effect as phthalates and in some cases it has shown to be superior to DEHP and DINP. Migration of SNS is lower than migration of DEHP and DINP. This is especially true for aqueous solutions, but a lower migration into lipids like sunflower oil is also observed.[3,12,58] The migration has been tested at different temperatures and it seems to be temperature independent.[4] It has tested to not be an eye or skin irritant, without sign of acute or chronic toxicity and without reproductive or hormone-disrupting effects.[12,56] It has no harmful effects on the environment.[12,58] Toxicity testing of SNS is done by looking at the no-observed-adverse-effect-level (NOAEL), in rats. This is about 1000 times higher for SNS than for DEHP.[28] The toxicity of SNS can be compared to corn oil. It shows no signs of mutagenicity and genotoxicity.[28]

The breakdown of SNS in humans has been evaluated with *in vivo* and *in vitro* studies. *In vitro* studies show no hydrolysis of SNS in salvia and gastric juice. Hydrolysis in pancreatin (pancreas fluid) is on the other hand observed, see results in Figure 1-10. The hydrolysis components were 12-acetoxy stearic acid (the free fatty acid), acetic acid and glycerol. It is noteworthy that the acetoxy group in the side chain is not hydrolyzed, even less when the glycerol is hydrolyzed off first. Hydrolysis products from hydrolysis of the glycerol backbone were insignificant, and these are therefore not displayed in Figure 1-10.[59]

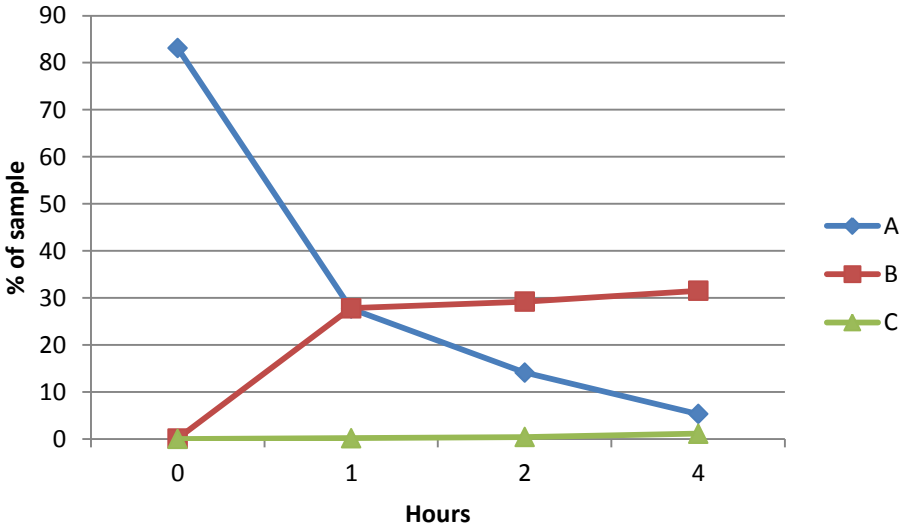



**Figure 1-10: Results of the *in vitro* tested pancreatic hydrolysis. Adapted from Sparsø and Jensen.[59] The structures of SNS (A), 12-acetoxy stearic acid (B) and 12-hydroxy stearic acid (C) are displayed in Figure 1-11.**

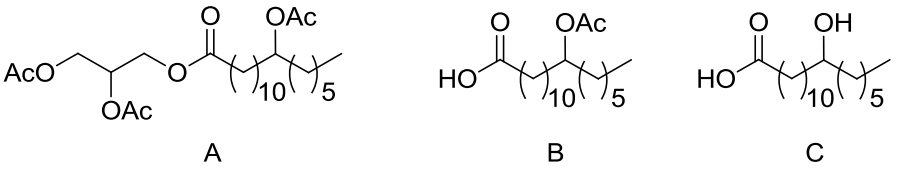



**Figure 1-11: Chemical structures of SNS (A), 12-acetoxy stearic acid (B) and 12-hydroxy stearic acid (C).**

By $^{14}C$ foot printing it was possible to study the *in vivo* absorption, distribution, metabolism and excretion of SNS. One study shows a dose relation in the rate of adsorption, meaning that it takes longer to adsorb a larger amount of SNS from the intestines. Another study showed that the acetylated glycerol backbone is hydrolyzed first in the intestines, leaving the 12-acetoxylated stearic acid, acetic acid and glycerol. 12-acetoxylated stearic acid can then later be hydrolyzed to 12-hydroxy stearic acid and acetate.[59]

In 2012 a life cycle assessment of SNS was released. This showed that SNS is truly a sustainable alternative, as it has low impact on water resources, greenhouse gas emissions and non-renewable resource depletion.[60,61] It contains no substances that are known to be hazardous to the environment.[62]

Because of its natural resource it was approved for food applications without any restrictions. Food quality is also about the wrapping of the food and increasing demands for sustainable or green alternatives to phthalates in the PVC wrapping are therefore important.[12] The use of SNS has been approved for use in contact with food in EU, USA, China and Japan. For the use in applications without further specific approval it has been approved in Switzerland, USA, Canada, China, Japan, South Korea, Brazil and Australia.[61]

SNS has been tested in several flexible PVCs for medical applications and has met all the requirements. In medical applications, SNS can be compared to DEHP or the newer alternatives tri(2-ethylhexyl) trimellitate or different polyadipates. The performance of SNS is significantly better than both of the other new alternatives.[12]

Also in toys, especially for children under the age of 3, it is important with a safe alternative. SNS has been tested in toys applications and have been approved as a fully functional alternative to phthalates. Shore A hardness is an often used parameter for efficiency in toys, and SNS has showed to have the same efficiency as DEHP in a wide range of plasticizer loading levels.[12] Shore A hardness is a measurement of the material's resistance to permanent indentation and was first described in the 1920s.[63]

The applications mentioned here are considered to be sensitive applications, where it is extra important to find alternatives to phthalates. But SNS could also be used in other less critical applications where for instance DEHP is used. These include vinyl flooring, wallpaper, textile dyes and sealants.

Different awards have been given to SNS. In 2005 SNS received the "Danish Industry Award"[64] and in 2006 is was the "Frost and Sullivan innovation award".[65,66] SNS has furthermore been nominated for the "Danish Society of Engineers award for innovation" in 2005 and for the "EU environmental award" in 2006.[55]

## 1.6 The Grindsted® SOFT-N-SAFE analogue

Although SNS is a really good alternative to phthalates, it is not a real substitute because of the price. It was therefore suggested to use the cheaper sun flower oil instead of castor oil. This would give the side chain acetoxy group in a 9- or 10 position as shown in Figure 1-12. Collectively these two compounds are known as the SOFT-N-SAFE-analogue (SNS-A). Initial application testing showed the same good results with SNS-A as SNS.[67]

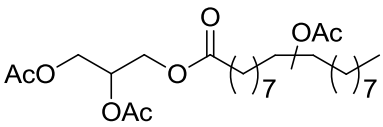



**Figure 1-12: Chemical structure of SNS-A. Notice the side chain acetoxy group can be either in the 9 or 10 position.**

Analysis of SNS-A *in silico* has shown that only small differences are observed between SNS and the two isomers of SNS-A and SNS-A can therefore be considered equally as safe to use as SNS. *In vitro* and *in vivo* tests confirm these results.[68]

The aim of the current project was to find a sustainable and cheap synthetic route to SNS-A.

# Chapter 2
# Short overview of the project

The project began with the findings of the good plasticizer effect of SNS and the following discovery of the equal good qualities of SNS-A by DuPont Nutrition Biosciences APS (legacy Danisco A/S). A cooperation between DuPont Nutrition Biosciences APS, Aarhus University (AU) and Technical University of Denmark (DTU) began with financial support from Danish Advanced Technology Foundation (Højteknologifonden).[6] The project was divided into four work packages which each had their own tasks. "Ionic liquids and ionic liquid-based technology with inorganic chemistry" was the headline for work package 1, which consisted of members from Department of Chemistry at DTU (DTU-Chemistry). The headline for work package 2 was "Ionic liquid-based technology with enzymatic catalysis". The members of work package 2 were from AU. Work package 1 and 2 had a close collaboration, and as the project moved on, work package 2 also took part in the inorganic catalysis. Work package 3 contained the members from DuPont Nutrition Biosciences APS and their task was "Process development, scaling up and product applications". Work package 4 worked independent of the rest of the work packages as their task was "Toxicity evaluation and safety concerns of products in food applications". It was members from Danish National Food institute at DTU (DTU-Food) who were responsible for work package 4.

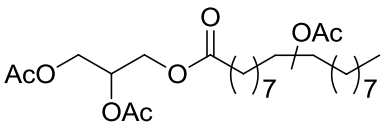



**Figure 2-1: Chemical structure of SNS-A, of which a synthetic pathway has been investigated in this PhD study.**

The overall goal of the project was to find and optimize a synthetic pathway for SNS-A.

## 2.1 Requirements and initial stretegies

DuPont Nutrition Biosciences APS had some requirements for the process that had to be fulfilled in order to make the project a success. The process had to be sustainable and cheap compared to the production of SNS. The first requirement is the starting material. SNS is produced from hydrogenatated castor oil, from castor oil (glycerol triricinoleate), which is rather expensive and not easily accessible compared to other oils.[69] This is due to the limited growth and harvesting conditions of the castor seeds, from the plant known as *Ricinus communis*, from where the castor oil is obtained.[70] The starting material for SNS-A, and thereby the starting point in this project, was glycerol monooleate (GMO), originated from high oleic sunflower oil (glycerol trioleate). In 2007 the production of sunflower oil was 9.9 Mt, which is high compared to the 0.6 Mt castor oil produced that year.[71]

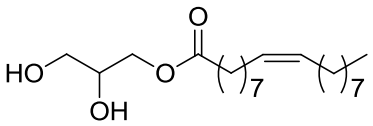



**Figure 2-2: Structure of glycerol monooleate (GMO).**

The production of SNS from the castor oil starts by hydrogenating the double bonds of the three fatty acids. It is then transesterified with glycerol to give the monoglyceride. The monoglyceride has three hydroxyl groups which are then acetylated to give SNS.[12,58,61] This is shown in Figure 2-3.

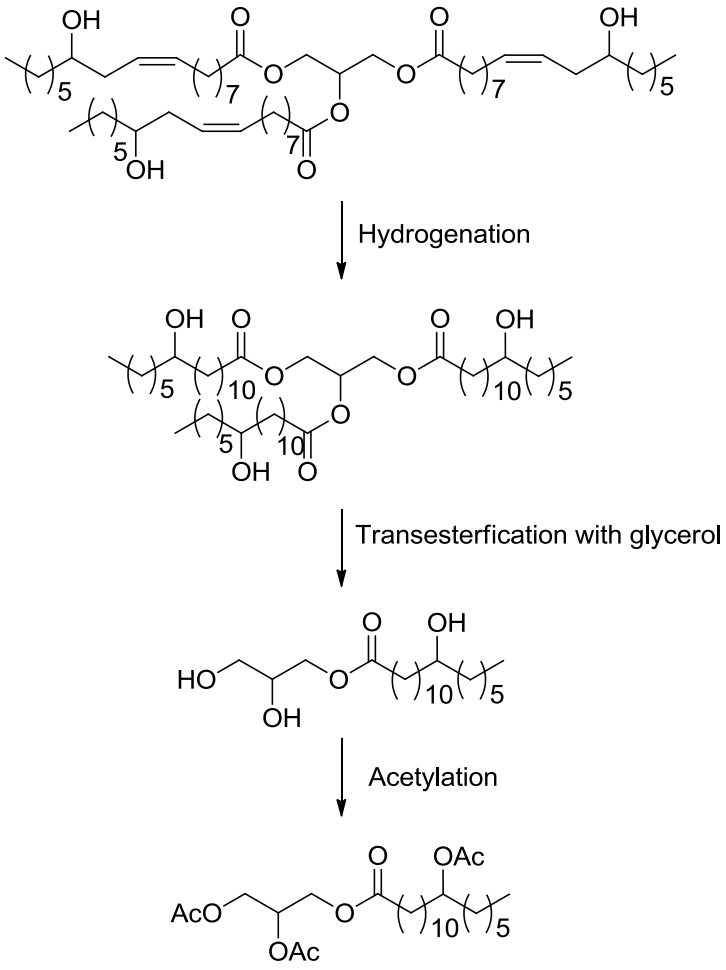



**Figure 2-3: Schematic overview of the synthesis of SNS. With inspiration from Danisco A/S.**[61]

For SNS-A the process starts with transesterification to give GMO. The double bond must then be functionalized to give the side chain hydroxyl group before acetylation. The initial ideas were to make a hydroxylation of the double bond followed by acetylation of the three hydroxyl groups or a direct acetoxylation of the double bond in combination with acetylation. This would give either a two-step process, just like the synthesis of SNS or a one-step process. The initial ideas are displayed in Figure 2-4.

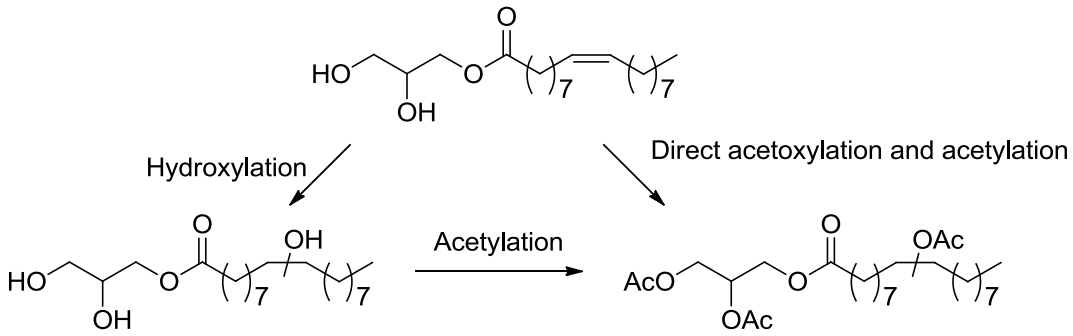



**Figure 2-4: Initial ideas of how to synthesize SNS-A from GMO were hydroxylation followed by acetylation (left side) or direct acetoxylation and acetylation (right side).**

It is also possible to start by acetylating of the glycerol backbone of GMO, giving diacetyl glycerol monooleate (DAGMO), and then functionalizing the double bond. The advantage of this is that it might be easier to functionalize the double bond without hydrolysis of the glycerol backbone when acetylated.[72] The disadvantage is the introduction of an extra step.

One other way of reducing the production costs is to use other reagents than used in the production of SNS. The acetylation step to produce SNS is done by using acetic anhydride, giving acetic acid as a byproduct. If the acetylation could be performed with acetic acid instead, this would give water as the byproduct, which is cheaper to dispose of afterwards. The price of acetic acid is also lower than that of acetic anhydride.[73] The disadvantage of this is the possibility of hydrolysis of the glycerol backbone to give the free fatty acid. From the beginning it was therefore clear that one of the important issues was to find a method for acetylating in acetic acid without hydrolysis. It was suggested to use a membrane process to remover water during the acetylation. The method is known as pervaporation and is a vacuum membrane distillation. The acetylation step was handled by others in the project.

The next challenge was the idea of a solvent free system. This has two direct advantages for the production costs, creating no expenses in adding or removing the solvent. Another advantage is the time saved in not having to

remove the solvent. Another way of avoiding this issue is by having a reaction media where the product is immiscible and therefore easily can be removed, to ease work-up. It was suggested to use an ionic liquid (IL), because of the possibility to adjust the solubility properties. The best would be to find an IL where the reactants were miscible in order to have faster reaction rate. The work with finding an IL is described in Chapter 3.

## 2.2 Initial modifications of glycerol monooleate

Much of the initial work in the project was focused on by others, but it is important to mention in order to understand the development of the project. The combined acetoxylation-acetylation of GMO was tested as one of the first things. This only resulted in the 9,10-dihydroxy glycerol monostearate (DHGMS) or hydrolysis. Also the hydroxylation of the double bond only resulted in hydrolysis. The initial ideas were therefore quickly discarded. Several oxidation methods were tested on both GMO and DAGMO were tested and it turned out that epoxidation of the double bond could be a possible. Enzymatic epoxidation was tested in different solvents, including different ILs. But the only satisfying result was obtained in dichloromethane and this method was therefore abandoned. Inspired by the epoxidation reaction in different ILs by L. Liu *et al*,[74] epoxidation with the *N*-butyl-*N*-methyl imidazolium ([BMIm]) based polyoxometalate $[BMIm]_3PW_{12}O_{40}$ as the catalyst was tested by co-workers in the project. Epoxidation of DAGMO in the IL $[BMIm]^+$ bis(trifluoromethylsulfonyl)amide ($[BMIm][Tf_2N]$) with hydrogen peroxide as the oxidant and air bubbling as a co-oxidant proved to be efficient. The problem then was that the product, 9,10-epoxy diaceyl glycerol monostearate (EDHGMS) was miscible with $[BMIm][Tf_2N]$ and had to be extracted. This gave two possible solutions: either to find an IL, which could separate out EDAGMS (see Chapter 3) or to test the system with GMO, as this is non-miscible with the IL (see Chapter 4). The BMIm based polyoxymetalate system will be further explained in Chapter 4.

As the most desirable process was the one with an acetylation reaction in the end, and not also in the beginning, the final suggested route for the synthesis of SNS-A was the three-step process shown in Figure 2-5.

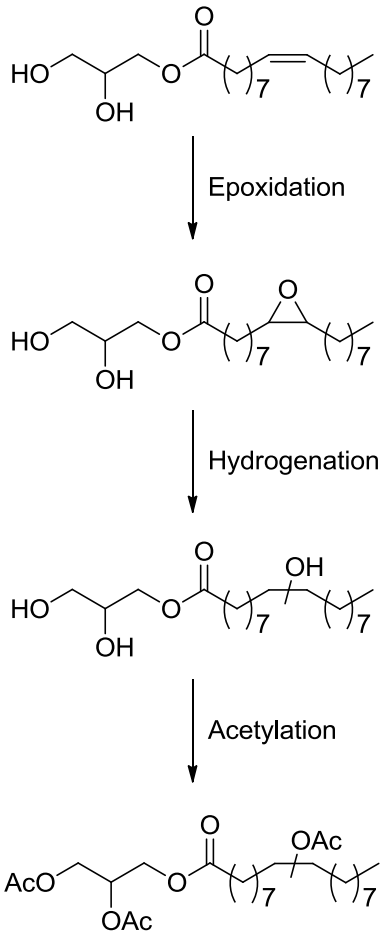



**Figure 2-5: Schematic overview of the final suggested reaction route: epoxidation, hydrogenation and acetylation to give SNS-A.**

The final suggested reaction route started with the epoxidation of GMO to 9,10-epoxy glycerol monostearate (EGMS). The epoxidation was tested with hydrogen peroxide or with peracetic acid as the oxidant. The second step was the reductive opening, or hydrogenation, of the epoxide to give either 9-hydroxy glycerol monostearate or 10-hydroxy glycerol monostearate. These compounds will collectively be known as monohydroxy glycerol monostearate (MHGMS). It was important to avoid ring opening to the DHGMS. The final step

was the acetylation of all three hydroxyl groups to give SNS-A. An overview of this can be seen in Figure 2-5.

## 2.3 Objectives of this PhD study

As mentioned earlier, the whole project has been a collaborative effort between several parties. However, only the parts of the project that I have been directly working on are highlighted in the thesis. The project can be divided into five parts:

1. The initial studies (e.g. hydroxylation or direct acetoxylation)
2. The IL separation system
3. Step one in the final route: non-enzymatic epoxidation
4. Step two in the final route: hydrogenation
5. Step three in the final route: acetylation

The first and the final part were handled exclusively by other participants in the project. The IL separation system consisted of three parts. Firstly was the synthesis of the ILs. Secondly was testing of miscibility with the starting material product and intermediates. Finally was the testing of epoxidation in the ILs in which EGMS or SNS-A was immiscible. The epoxidation work was started by a co-worker, but mostly using DAGMO as substrate. The epoxidation of GMO, with inorganic catalysts were investigated from the good results with DAGMO, primarily by me, whereas the epoxidation with peracetic acid was conducted exclusively by me. The hydrogenation work can be divided into two separate parts: hydrogenation using hydrogen gas and hydrogenation using a sacrificial hydrogen donor source. The hydrogenation with hydrogen gas can again be divided into two parts: hydrogenation after a using an inorganic catalyst and hydrogenation after epoxidation with peracetic acid. The hydrogenation after the catalytic process was handled solely by others, while the hydrogenation after the peracetic acid based process was handled mostly by me. The hydrogenation with the hydrogen donor was performed by me.

# Chapter 3
# The ionic liquid separation system

ILs had a central role from the beginning of the project. As a separation solvent, it was anticipated to work as a reaction media for one or more of the reaction steps and then be able to separate out the reaction product. It was important that the IL should only be a helping agent and not be consumed in the process. This was important as the IL should be reused to keep production costs low. Work has been done on finding an IL with this separation ability and ILs which separated out any of the products were tested in the epoxidation reaction.

## 3.1 Introduction to ionic liquids

ILs are salts that are liquid at ambient temperatures, with melting points less than the boiling point of water (100 °C).[75–77] A subcategory is the room temperature ILs (RTILs) which are liquids at room temperature.[78] The most common ILs contain one of the five cations: imidazolium, ammonium, pyrrolidinium, pyridinium or phosphonium (see Figure 3-1). The substituents of the cations, known as R, R', R'' and R''' are often alkyl chains, but may also contain functionalized chains or rings. This includes fluoroalkyl, alkenyl and methoxy among others. The melting point of the IL is often higher if the anion is halide or bulky because of stronger ionic boning. Increasing the length of the alkyl chain on the cation will also in general increase the melting point.[76]

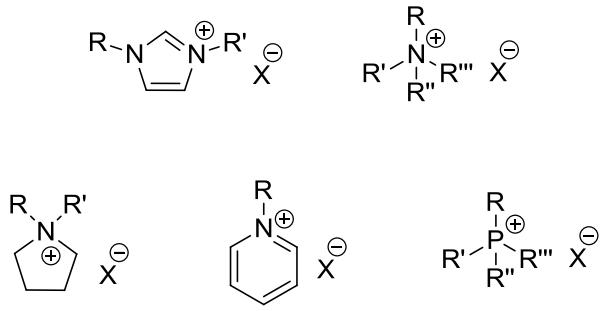


**Figure 3-1: Chemical structures of the most common ILs. Top left: imidazolium, ammonium, Bottom left: pyrrolidinium, pyridinium and phosphonium. R, R', R'' and R‴ are often alkyl chains, but can also be functionalized groups. $X^-$ is the anion.**

ILs can act as solvents for a broad spectrum of chemical reactions and can sometimes have a dual function as both catalyst and solvent.[79] Another important property of ILs is the extremely low vapor pressure[79] and the high polarity, not to be confused with hydrophilicity, of the ILs.[78] The low vapor pressure makes the ILs easier to efficiently reuse, because of lower emission of solvent.[80] This has also caused the ILs to be known as green alternatives to organic solvent.[81] Reduction of the emission of solvent would be very beneficial for the envirionment.[76] ILs often have a wide liquid range, up to 400 °C,[82] making reactions in the certain IL possible at a wide range of temperatures. Physical properties like density and viscosity is also worth mentioning.[75,79] Normally the viscosity is higher when the IL has long alkyl chains in the cation and a large anion.[75]

The miscibility with organic compounds can often be changed by varying the chain length of the alkyl substituents on the cation because of altered polarity. On the other hand, it is often the anion that determines the chemical properties of the IL. In this way it is, in theory, possible to design the IL to fit to the chemical reaction wanted by choosing the right building blocks.[75,78,79,81] By tuning the IL to be immiscible with the reactants, but miscible with the catalyst, it is possible to have the benefits from both homogeneous and heterogeneous catalysis. This include mild reaction conditions and high efficiency and selectivity from homogeneous catalysis with easy catalyst separation from heterogeneous catalysis.[79] Water miscibility is often

determined by the anion, the cation only having a secondary effect. It is important to note that the hydrophobic ILs often are hygroscopic, meaning they can absorb water from atmospheric air. This can be an issue if the reactions are conducted with moisture-sensitive reactants.[82]

The syntheses of ILs are often very simple. Often a simple quaternization reaction is sufficient, giving $[NR_3R']^+X^-$ in the top part of Figure 3-2. If it is not possible to obtain the desired anion this way, there are typically other alternatives. Adding a Lewis acid $MX_y$ to give the anion $MX_{y+1}^-$, adding a metal salt MA and remove MX to form the anion $A^-$, adding a Brønsted acid HA and evaporate HX to give the anion $A^-$ or by ion exchange resin. This is seen in the bottom part of Figure 3-2.[83] The desired cation is often commercially available as the halide salt and only anion exchange is necessary. If not, the formation of the cation can be carried out by reaction with the desired alkylhalogenid in the quarternization step. This is also a way of functionalizing the IL.[77]

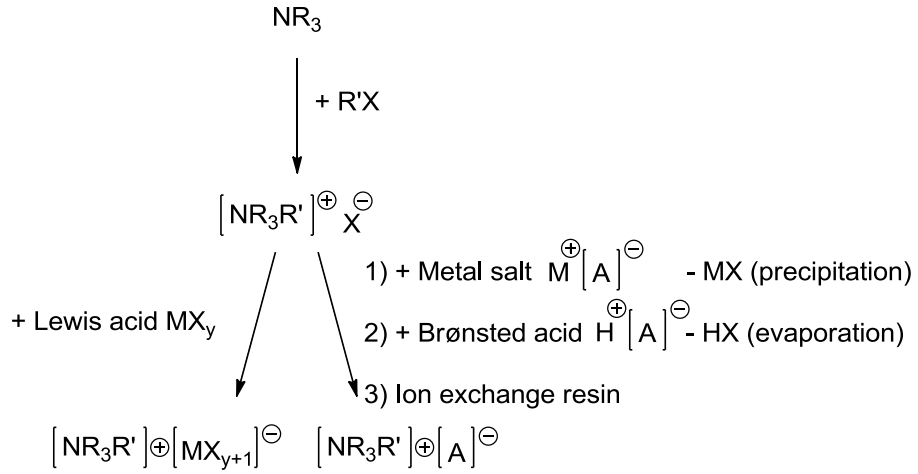



**Figure 3-2: Simplified scheme for the synthesis of ILs, exemplified for an ammonium salt. $R_3$ can be three identical R groups or different. Adapted from Wassersheid and Keim.[83]**

After synthesis, purification is needed. But because of the low vapor pressure, distillation is not an option. Low melting points make purification by crystallization difficult. For water-immiscible ILs washing with water after finished reaction is a possibility to remove water-miscible byproducts.[77]

## 3.2 Desired properties

As briefly described in Chapter 2, an IL in which the product was not soluble was desired, ensuring the product can be obtained by simple phase separation. This product could either be the end product (SNS-A) or a product from one of the initial steps i.e. EGMS or MHGMS. It was preferred that GMO was miscible with the chosen IL to have a faster reaction. It was important that the melting point of the IL not was higher than the desired reaction temperature to enable the IL to act as solvent and that the IL can easily be recycled. Furthermore, it was also important for the IL to be non-miscible with water in order to avoid hydrolysis of the glycerol backbone. It was therefore suggested to use ILs with the anion $[Tf_2N]^-$, as these in general are hydrophobic.[77] This way, focus would be to find the right cation.

## 3.3 Synthesis of ionic liquids

The synthesis of ILs in the project can be divided into four steps: synthesis of ether functionality, addition of substituents to imidazolium based ILs, addition of substituents to phosphonium based ILs and anion exchange to $[Tf_2N]^-$. All synthetic protocols are described in the Experimental section.

### 3.3.1 Synthesis of ether functionality

Two different ether containing substituents were prepared according to Riisager *et al* to be incorporated into the IL in the second step.[84]

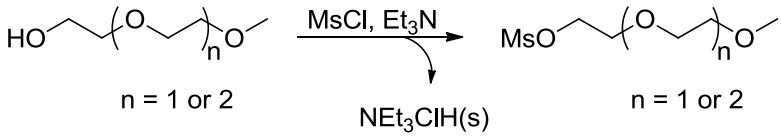



**Figure 3-3: Schematic overview of the synthesis of ether functionality according to Riisager *et al*.**[84]

The mesylates were synthesized by reaction of the alcohol with mesyl chloride in the presence of triethylamine, yielding the mesylate and triethylammonium

chloride. Both mesylates were obtained in high yields (> 99 %) and characterized by NMR. NMR indicated high purity of the mesylates.

### 3.3.2 Addition of substituents

One or two octyl substituents have been added to imidazole or 2-methylimidazole by octyl bromide. Addition of two octyl groups resulted in the bromide ionic liquids which later were anion exchanged with $LiNTf_2$. This work was performed with inspiration from the work of Khabmadideh *et at*.[85] Two octyl groups were added over two steps to imidazole, yielding 1-octylimidazole as an intermediate product in 90 % yield and high purity according to NMR.

Addition of the ether substituent prepared in section 3.3.1 depends on the substituents on imidazole and was inspired by Riisager *et al*[84] or Huang *et al*.[86] ILs with two ether substituents or with either a methyl or octyl substituent have been prepared. Addition of two ether containing substituents to 2-methylimidazole was done in one step with inspiration from Buaki *et al*.[87] The intermediates 1-(2-(2-methoxyethoxy)ethyl) imidazole and 1-(2-(2-(2-(methoxyethoxy)ethoxy)ethyl) imidazole were synthesized in 87 % and 96 % yield respectively, although for the last compound, impurities from solvent was detected by NMR analysis.

The addition of an ester containing group as substituent was inspired by the work of Khabnadideh *et al*[85] and Gathergood *et al*.[88]

In addition to the imidazolium based ILs, two different phosphonium based ILs have been prepared, with either the ether functionality described in chapter 3.3.1 or an ester functionality. The addition of an ether functionality was inspired by Gathergood *et al*[88] and the addition of an ester functionality was inspired by Ermolaev *et al*.[89]

### 3.3.3 Anion exchange to $[Tf_2N]^-$

As briefly mentioned earlier, it was decided early in the project to focus on ILs with the anion $[Tf_2N]^-$ because of high hydrophobicity. All ILs therefore had to go through an anion exchange. The anion exchange was performed with $LiTf_2N$. This work was inspired by Riisager *et al*.[84] or Bonhôte *et al*.[90] Many of the ILs were anion exchanged before characterization.

## 3.4 Overview of ILs

18 different ILs were synthesized for miscibility testing. The first IL synthesized and tested was [BMIm][$Tf_2N$] as briefly introduced in chapter 2.2. This was synthesized from [BMIm]Cl by anion exchange with $LiTf_2N$ in high yield (>99 %), though impurities from the solvent was detected by NMR analysis. Here is on overview of the other cations used:

Eight different imidazolium based ILs with at least one ether functionalization were synthesized:

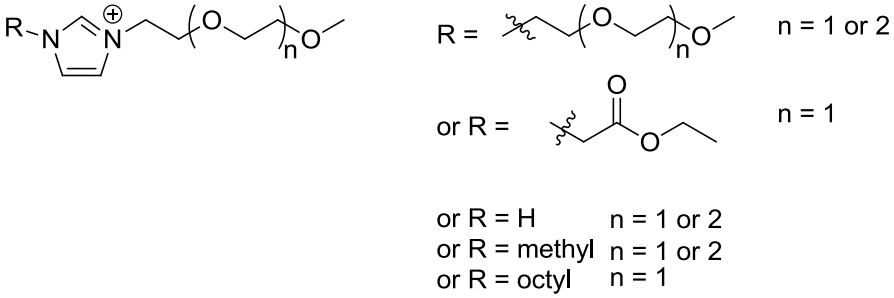



**Figure 3-4: overview of the cations which are imidazolium based with one of the substituents being ether functionalized.**

The two ILs with two ether functionalities were synthesized in 80 % and 89 % yield respectively. Characterization by NMR analysis revealed solvent impurities. The mixed ether and ester functionalized IL was synthesized in 67 % yield and high purity according to NMR analysis. Attempts to purify the IL were not performed. The two protic ILs were synthesized in 85 % yield for the short ether chain and 62 % for the long ether chain. NMR analysis indicated high

purity of these ILs. The methyl substituted ILs were synthesized in very high yields (>99 %), but NMR analysis revealed impurities in both ILs. Attempts to purify the IL were not performed. The octyl substituted IL was synthesized in 71 % yield and high purity according to NMR analysis.

Besides the cation with one ether functionality and one ester functionality (see Figure 3-4), two different imidazolium based with one of the substituents being ester functionalized was synthesized:

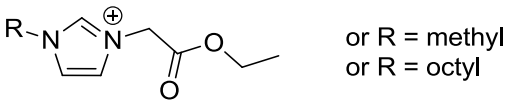



**Figure 3-5: Overview of the imidazolium based cations with one of the substituents being ester functionalized.**

These two ILs were synthesized in 99 % yield for the methyl substituted IL and 61 % for the octyl substituted IL. The methyl substituted IL had, according to NMR analysis, impurities, whereas the octyl substituted IL was found to have high purity according to NMR analysis.

Besides the *N*-octylimidazolium based cations described above, two others have been synthesized:

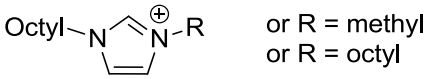



**Figure 3-6: Overview of the *N*-octylimidazolium based cations.**

The methyl substituted IL was synthesized in very high yield (>99 %), but according to NMR analysis, not in with high purity. It was not attempted to further purify the IL. The IL 1,3-dioctyl imidazolium bis(trifluoromethylsulfonyl)amide was synthesized in 73 % yield over two steps from 1-octylimidazole. NMR analysis indicated high purity.

Three different 2-methylimidazolium based cations were synthesized:

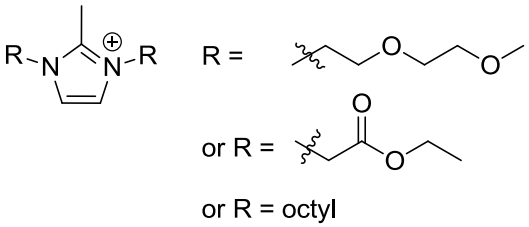



**Figure 3-7: Overview of the 2-methylimidazolium based cations.**

The IL containing two ether functionalized substituents was synthesized in very high yield (>99 %), but NMR analysis indicated high impurity. It was not attempted to further purify the IL. The ester containing IL was synthesized in three steps, as the ester containing substituents were added one at a time. The yield of the IL was 35 % over three steps. NMR analysis indicates high purity. The IL with two octyl substitutent was synthesized by addition of both octyl substituents in one step, followed by anion exchange. This was synthesized in >99 % yield, though NMR analysis indicated some solvent was still present in the IL.

In addition to the imidazolium based ILs, two phosphonium based cations were synthesized:

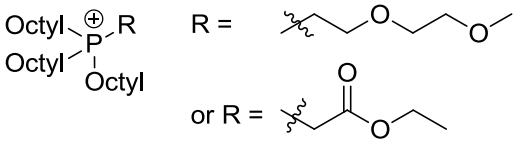



**Figure 3-8: Overview of the phosphonium based cations.**

The two phosphonium based ILs were synthesized in 77 % over two steps for the ether containing substituent and 82 % yield over two steps for the ester containing substituent. Both ILs were synthesized with high purity according to NMR analysis.

Furthermore, ILs with the following cations have been purchased from Iolitec[91] for miscibility testing:

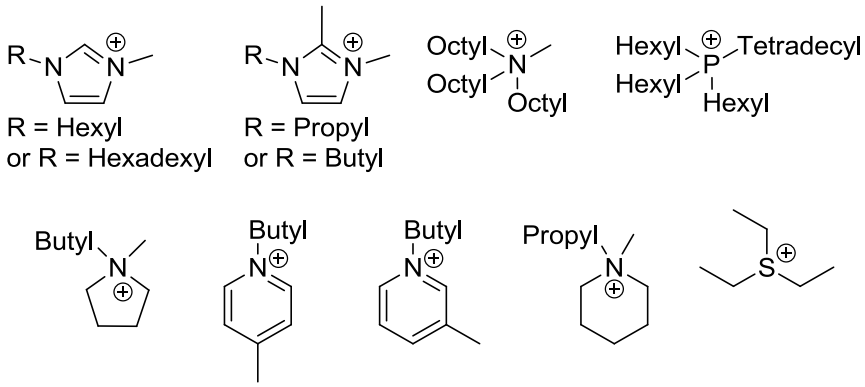


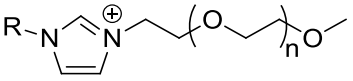
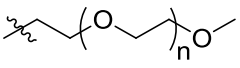
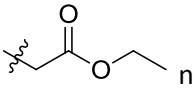
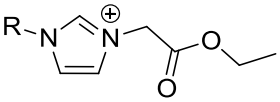
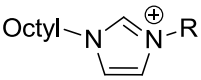
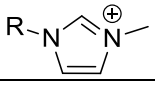
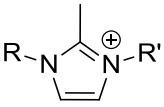
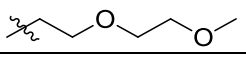
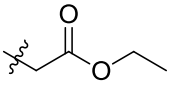
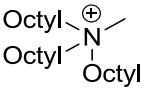

**Figure 3-9: Overview of purchased ILs from Iolitec[91] for miscibility testing.**

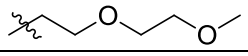
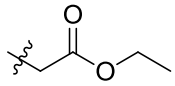
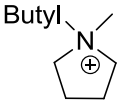
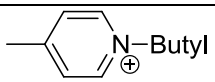
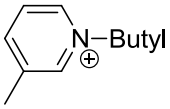
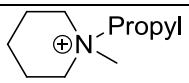
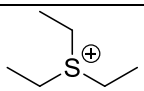
The top row of ILs displayed in Figure 3-9 were chosen because of similarities with the synthesized ILs. The ILs displayed in the bottom row was tested to look at other backbone skeletons than the ones synthesized.

## 3.5 Trends in miscibility testing of ionic liquids

The result of the miscibility tests is shown in Table 3-1. The miscibility testing was performed by miscing the substrate and the IL in a 1:1 volume ratio. The numbers (1 or 2) indicate how many phases the substrate and IL formed after mixing. ND means not determined. The testing is based on qualitative results, i.e. does the IL and substrate form one or two phases when mixed. If the IL shows good qualities in the miscibility tests, it will be tested in the epoxidation reaction of GMO to EGMS. If this also gives good result, the miscibility tests will be done quantitatively to ensure that separation is possible.

**Table 3-1: Overview of the miscibility tests. 2 = 2 phases, 1 = 1 phase, ND = not determined**

| Cation | | GMO | EGMS | MHGMS | SNS |
|---|---|---|---|---|---|
| BMIm | | 2 | 2 | ND | 1 |
|  | R =  n = 1 or 2 | 2 | 2 | 2 | 1 |
| | R =  = 1 | 2 | 2 | ND | ND |
| | R = H, n = 1 or 2 | 2 | 1 | 1 | 1 |
| | R = Methyl, n = 1 or 2 | 2 | 1 | 1 | 1 |
| | R = octyl, n = 1 | 2 | 2 | 1 | ND |
|  | R = Methyl | 2 | 2 | 2 | 1 |
| | R = Octyl | 1 | 1 | 1 | 1 |
|  | R = Methyl | 2 | 1 | 1 | ND |
| | R = Octyl | 1 | 1 | 1 | 1 |
|  | R = hexyl | 1 | 1 | 1 | 1 |
| | R = Hexadecyl | 1 | 1 | 1 | 1 |
|  | R = R' =  | 2 | 1 | 1 | 1 |
| | R = R' =  | 2 | 2 | 2 | ND |
| | R = R'= Octyl | 2 | 1 | 1 | ND |
| | R = Methyl, R' = Propyl | 2 | 2 | 2 | 1 |
| | R = Methyl, R' = Butyl | 2 | 1 | 2 | 1 |
|  | | 1 | 1 | 1 | 1 |

| Cation | | GMO | EGMS | MHGMS | SNS |
|---|---|---|---|---|---|
|  | R = Octyl, R' =  | 2 | 1 | 1 | ND |
| | R= Octyl, R' =  | 2 | 1 | 1 | ND |
| | R= Hexyl, R' = Tetradecyl | 1 | 1 | 2 | ND |
|  | | 2 | 1 | 1 | 1 |
|  | | 1 | 1 | 1 | 1 |
|  | | 2 | 1 | 1 | 1 |
|  | | 2 | 1 | 2 | 1 |
|  | | 2 | 2 | 2 | 1 |

From Table 3-1 it can be seen that all the tested ILs were miscible with SNS. This means that separation must take place before the final step. Often GMO was immiscible with the IL as the only substrate. This was the opposite of what was wanted. If EGMS was immiscible with the IL, then GMO was immiscible with the tested IL. Almost the same trend was observed for MHGMS when compared with GMO. The exception was the trihexyl tetradecyl phosphonium based IL. The other phosphonium based ILs did not show the same trend, but this could be due to the higher polarity of the ether- and ester substituted ILs EGMS and MHGMS were almost miscible with the same ILs.

If only alkyl chains were present in the IL, like two long nonpolar groups as the octyl group GMO showed to be immiscible with the IL. Having a methyl group as one of the substituents makes the IL miscible with GMO. This must be due to the shorther chain makes the IL more polar and thereby miscible with GMO.

Addition of two ether groups to imidazolium makes the ILs polar enough to be immiscible with GMO, EGMS and MHGMS. Having only one ether group and a proton or an alkyl substituent makes the IL only immiscible with GMO. The exception is if the other substituent was octyl, where EGMS also was immiscible. This looks like an error has occurred in the testing, as adding a non-polar group should not make the IL less miscible with EGMS.

Addition of an ester group together with an ether group or a short alkyl chain makes the ILs immiscible with GMO and EGMS. Adding a non-polar group as an octyl chain is enough to reverse the polar effect of the ester group, making the IL miscible with all the substrates.

By adding a methyl group in the 2-position of the imidazole, the slightly acidic proton was removed. This could be an advantage for the reactions performed in the IL, as the hydrolysis of the glycerol backbone is catalyzed by acids. Addition of two very polar groups makes GMO immiscible with the IL. Alkyl chains make the IL immiscible with GMO as well. This was not expected as the non-polar alkyl chains should make the ILs and substrates miscible, but the alkyl chains were short enough to not have this effect.

For the phosphonium based ILs it was observed that it needs long non-polar groups to be immiscible with MHGMS. This was unexpected as the results from imidazolium indicate long alkyl chains make the IL miscible with all the substrates. The ether and ester groups make the IL more polar, but not polar enough to make the IL immiscible with either EGMS or MHGMS. The immiscibility could also be due to the slightly longer alkyl chains compared to the first described IL, making the IL less polar.

Looking at ILs not containing either imidazolium or phosphonium, it was only triethyl sulphonium and the piperidinium based ILs that had the miscibility properties that could be used in this project.

The miscibility of the substrate in some the ILs were calculated by project partners from AArhus University by the “conductor like screening model for real solvents” (COSMO-RS) model.[92] This models can calculate the trends of solubility of different compounds in different solvents. The calculations were performed at both RT and 60 °C. Prediction showed the same trend as

observed, that EGMS is more soluble in [BMIm][$Tf_2N$] than GMO, and increasing the temperature makes both substrates more miscible with the IL. The ether functionalized ILs tested were, according to the calculations, less miscible with the IL than GMO in the ether functionalized ILs.

# Chapter 4
# Catalytic epoxidations

The first step in the final suggested process route is the epoxidation of GMO to EGMS as displayed in Figure 4-1. This work was initiated by another participant in the project and includes the use of an inorganic catalyst. Besides catalytic epoxidations with an inorganic catalyst, enzymatic epoxidation has also been investigated by others in the project. These results will be evaluated elsewhere and not commented further here.

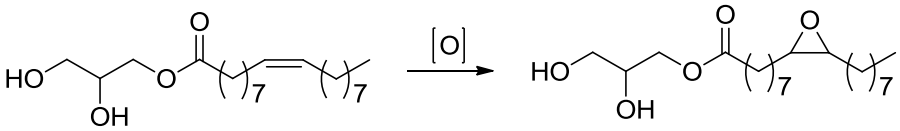



**Figure 4-1: GMO is epoxidized to EGMS.**

Epoxidation of olefins are often performed by reaction with a peroxide containing reagent, which can donate a single oxygen atom. Hydrogen peroxide or peroxycarboxylic acids are the most common peroxide reagents. This chapter describes the work with catalytic epoxidation using hydrogen peroxide, whereas the next chapter describes the work with peracetic acid.

Using hydrogen peroxide or alkyl hydroperoxides needs a catalyst, often a transition metal, to initiate epoxidation reaction. Epoxidation of oils often involves a strong acid catalyst.[93] The transition metal can also help directing an asymmetrical epoxidation. Sharpless (sometimes referred to as Sharpless-Katsuki) asymmetric epoxidation describes the first known general asymmetric epoxidation catalyst.[94] This work described the epoxidation of an allylic alcohol, having the alcohol directing the epoxidation. The Jacobsen (sometimes referred to as the Jacobsen-Katsuki) epoxidation is one way of describing the

asymmetric epoxidation of unfunctionalized alkenes.[95,96] When using hydrogen peroxide as the oxidant, the byproduct is water, as seen in Figure 4-2. This could be a problem here, as water could hydrolyse the ester bond in GMO to give the free fatty acid and glycerol.

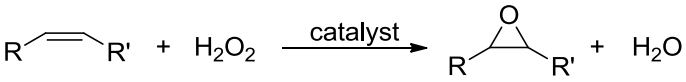



**Figure 4-2: Epoxidation using hydrogen peroxide gives water as byproduct.**

The use of diluted hydrogen peroxide with a functionalized heteropoly acid (HPA) working as a phase transfer catalyst for epoxidations of olefins in known as Ishii-Ventrillo chemistry and has been widely described in literature.[97–101] Using a phase transfer catalyst could be the solution for the hydrolysis problems, as the substrate and product is not in contact with the aqueous phase as suggested by Ishii *et al*[97] and displayed in Figure 4-3.

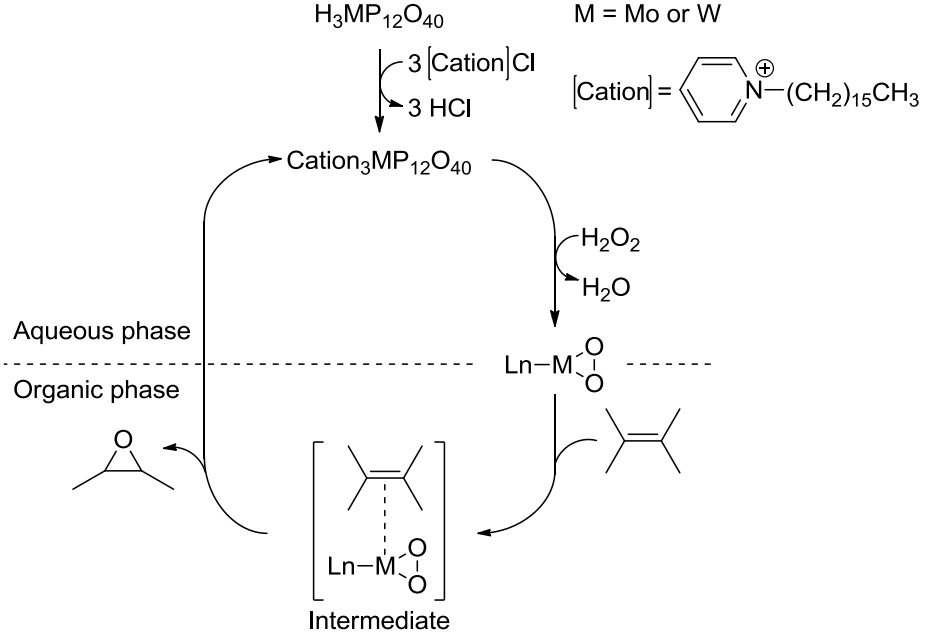



**Figure 4-3: Suggested mechanism of the phase transfer action of the catalyst. Adapted from Ishii *et al*.**[97]

The HPA is reacted with an IL to give the active catalyst (described as $Cation_3MP_{12}O_{40}$) in Figure 4-3. This is done in the aqueous phase. The catalyst then reacts with aqueous hydrogen peroxide to give water and an active species that is transferred to the organic phase. This species can then react with the olefin to give the epoxide and the catalyst, which is transferred back to the aqueous phase, to go into a new catalytic circle.

One problem of this reaction is the use of an organic solvent, often $CH_2Cl_2$ or $CHCl_3$, which are carcinogenic and toxic.[102,103] Furthermore, catalyst recovery has proven difficult. It has therefore been suggested to use IL instead. Oxidation of alcohols with a phosphotungstate complex in an IL was described in 2005[104] and in 2007 epoxidation in IL was described.[74] The epoxidation in IL is described in Figure 4-4.

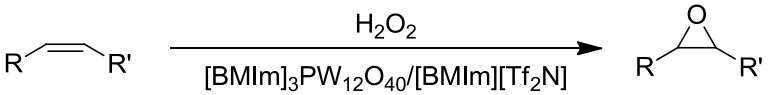



**Figure 4-4: Epoxidation using $H_2O_2$ and a phosphotungstate complex in the IL [BMIm][$Tf_2N$]. Adapted from Liu *et al*.**[74]

Liu *et al* tested different substrates and solvents, mostly ILs and one of them was [BMIm][$Tf_2N$] as displayed in Figure 4-4. This was interesting for this project, as it was agreed to use an IL with this anion. The reaction time was short for the alkenes tested, only 1 hour, and reaction temperature was 60 °C.

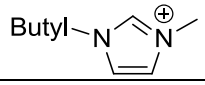
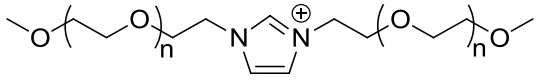
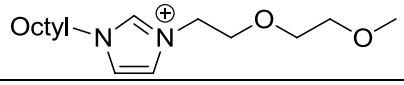
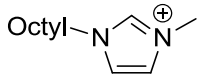
## 4.1 From previously experiments

The work by Liu *et al* inspired us to examine the epoxidation protocol in the project.[74] Most of the initial work was performed with DAGMO as the substrate or using the test substrate cyclooctene oxide. Different ILs and catalysts were tested and the best turned out to be [BMIm][$Tf_2N$] and $[BMIm]_3PW_{12}O_{40}$. One problem with this was that the resulting epoxidized DAGMO (EDAGMS) must be extracted from the reaction mixture with hexane as it was miscible with the IL. The best result in small scale of epoxidation of DAGMO was done with 0.36 mL DAGMO to 1 mL [BMIm][$Tf_2N$], 1.5 eq $H_2O_2$

and 0.003 eq catalyst. The reaction mixture was stirred at 60 °C for 24 hours. This resulted in 90 % EDAGMS, determined by GC analysis. Upscaling of this procedure gave problems with low conversion to EDAGMS. It turned out that streaming air into the system, adding the hydrogen peroxide over time and lowering the amount of hydrogen peroxide to 1.1 eq improved the results. Additionally, the reaction time was also shortened to 1.5 hours. The best result from upscaling to 10.8 mL DAGMO in 30 mL [BMIm][$Tf_2N$] was a conversion of 98 % to EDAGMS after 1.5 hours. After 4 hours reaction time, only trace amounts of DAGMO were left. When up scaling the experiments it was easy to see the phase separation between the organic and the aqueous phase. Furthermore it was noticed that the catalyst was dispensed and not dissolved in either phases. This could be beneficial when looking at catalyst recycling later.

Initial testing of the epoxidation of GMO with this system gave only poor or no conversion. Some of the ILs described in Chapter 3 was also tested. The results are described in Table 4-1.

**Table 4-1: Overview of the initial result of epoxidation of GMO in different ILs.**

| IL | | Result |
|---|---|---|
|  | | Low or no conversion |
|  | n = 1 | Only an unknown product was observed |
| | n = 2 | Hydrolysis |
|  | | No conversion |
|  | | No conversion |

As displayed in Table 4-1 no good result with GMO has been obtained in any of the four ILs. Low or no conversion was observed, which could be due to a low

reaction rate because of the heterogeneous reaction system. Hydrolysis could be due to the substrate was not miscible with the IL and therefore not protected from the water from the hydrogen peroxide. The unknown product formed in one IL could be degradation of the substrate.

## 4.2 Preparation of different catalysts

The catalyst used so far contained the $[BMIm]^+$ cation. But to determine the effect of the cation, if any, catalysts having all the cations from the ILs not tested so far were synthesized. It should be noted that one IL was eliminated due to a melting point being higher than the reaction temperature of 60 °C. This is the IL displayed in Figure 4-5

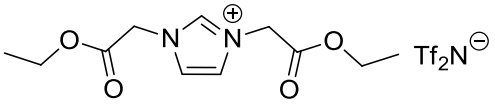



**Figure 4-5: Chemical structure of the eliminated IL due to too high melting point.**

This left 8 different cations to be built into the catalyst. These are displayed in Figure 4-6.

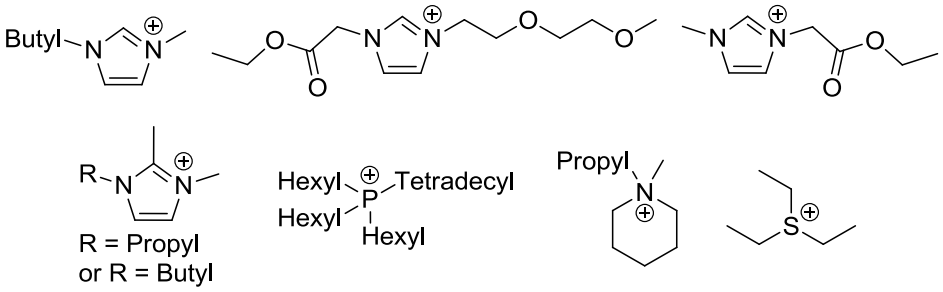



**Figure 4-6: Chemical structures of the cations incorporated into the catalyst.**

The synthesis procedure was similar to the one described by Chiang *et al*.[105] One catalyst, (1-butyl-2,3-dimethyl imidazolium)$_3PW_{12}O_{40}$, resulted in a low

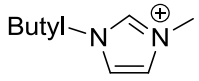
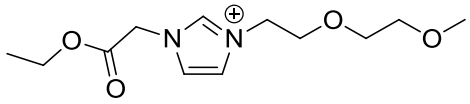
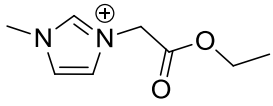
yield (33 %) but otherwise the yield was 65-85 %. The catalysts have not been characterized before testing in the epoxidation reaction.

## 4.3 Test of different ionic liquids and catalysts

Both DAGMO and GMO were tested in the epoxidation reaction in different ILs. DAGMO was tested only with the $[BMIm]PW_{12}O_{40}$ catalyst, whereas GMO was tested with two different catalysts, containing either the $[BMIm]^+$ cation or the same cation as the IL tested. The results are summarized in Table 4-2 (for DAGMO) and Table 4-3 (for GMO). Epoxidation of DAGMO in $[BMIm][Tf_2N]$ was however performed to test the activity of the catalyst, which showed the predicted result.

The epoxidation was tested with 0.003 equivalents of catalyst, 1.1 equivalents of $H_2O_2$ at 60 °C, as this gave the best result with DAGMO.

**Table 4-2: Overview of results of the epoxidation of DAGMO in different ILs. The catalyst contained the $[BMIm]^+$ cation regardless of the cation in the solvent. Samples were taken after 1 h, 3 hours and 20 hours, except for $[BMIm][Tf_2N]$ where a sample was taken after 24 hours.**

| Cation in IL | result |
|---|---|
|  | 90 % EDAGMS was observed after 24 hours. This was tested by a co-worker. |
|  | Mostly non-converted material was observed, but some EDAGMS was also observed. Already after 1 hour was hydrolysis a problem, and after 20 hours it was the main reaction observed. |
|  | Mostly EDAGMS was observed, already after 1 hour. There was still almost as much DAGMO present. After 20 hours, hydrolysis became a problem. Still some DAGMO was left unconverted. |

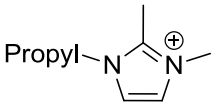
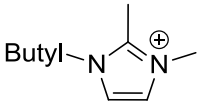
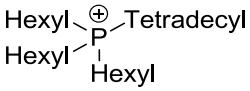
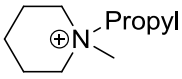
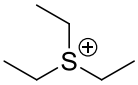
| Cation in IL | result |
|---|---|
|  | The only conversion observed was hydrolysis, already after 3 hours, hydrolysis was the major reaction observed. There was no sign of EDAGMS. |
|  | The only conversion observed hydrolysis, already after 1 hour hydrolysis products were the main product observed, though the amount did not further increase during reaction. There was no sign of EDAGMS. |
|  | Small amounts of EDAGMS were observed, but mostly unconverted material and hydrolysis was observed. |
|  | After 1 and 3 hours was the only conversion observed a bit of hydrolysis, but after 20 hours traces of EDAGMS was observed, although mostly unconverted, but also hydrolyzed compound was observed. |
|  | The only conversion observed was hydrolysis. Mostly unconverted material was observed. |

Table 4-2 gives an overview of the results of epoxidation of DAGMO in different ILs. With three of the ILs, no conversion, except hydrolysis was observed. This was the two different 2-methylimidazolium based ILs and the sulphonium based IL. This could be due to poor solubility of the substrate in the IL.

The two other imidazolium based ILs tested showed better results. The one with an ester and an ether functionality showed still mostly unconverted material, but some EDAGMS was also observed. With a methyl group and an

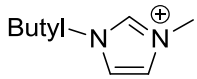
ester functionality, mostly EDAGMS was observed, but not as promising as the results previously obtained using [BMIm][$Tf_2N$] as solvent.

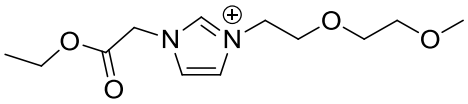
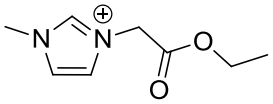
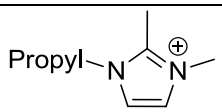
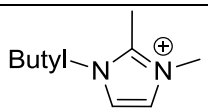
With the piperidinium based IL, some EDAGMS was observed, but primarily unconverted or hydrolyzed material was observed. The phosphonium based IL showed the same trend. Water from the hydrogen peroxide must be easier accessible, this must be due to poor solubility of the substrate in the ILs.

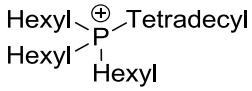
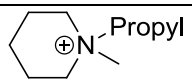
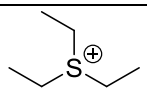
From these tests, the best IL for the epoxidation of DAGMO to EDAGMS was the IL originally used, namely [BMIm][$Tf_2N$].

It was furthermore tested to epoxidize DAGMO with no solvent present. This resulted in no formation of EDAGMS, but only hydrolysis and epoxidation of the free fatty acid.

**Table 4-3: Overview of results of the epoxidation of GMO in different ILs. Notice that the catalyst contains either the [BMIm]$^+$ cation or the same cation as the solvent. Samples were taken after 1 hour, 3 hours and 20 hours.**

| Cation in IL | Cation in catalyst | Result |
|---|---|---|
|  | [BMIm]$^+$ | Conversion to EGMS was observed, although mostly starting material was observed. The conversion to EGMS was 24 % after 3 hours and the amount was not further increased. Unconverted material was 73 % after 3 hours. |

| Cation in IL | Cation in catalyst | Result |
|---|---|---|
|  | $[BMIm]^+$ | Only small conversion to EGMS (15 %) was observed after 20 hours. Most of the product was unconverted starting material (81 %) |
| | As IL | After 20 hours, the amount of EGMS was almost the same as the amount of starting material (42 % and 45 % respectively). Hydrolysis was also a problem (10 %). |
|  | $[BMIm]^+$ | After 20 hours the amount of EGMS and GMO was almost equal (42 and 43 % respectively), but DHGMS was also a problem (10 %). |
| | As IL | After 1 and 3 hours no conversion was observed, but after 20 hours, both EGMS (22 %) and DHGMS (5 %) were observed. Also hydrolysis was observed (6 %). |
|  | $[BMIm]^+$ | No reaction was observed |
| | As IL | No reaction was observed |
|  | $[BMIm]^+$ | No reaction was observed |
| | As IL | No reaction was observed |

| Cation in IL | Cation in catalyst | Result |
|---|---|---|
|  | $[BMIm]^+$ | The only observation was to DHGMS (10 % after 20 hours). There was no sign of EGMS. Mostly unconverted starting material was observed (85 %) |
| | As IL | The only observed conversion was to DHGMS (7 % after 20 hours). There was no sign of EGMS, and still mainly starting material was observed (90 %). |
|  | $[BMIm]^+$ | No reaction was observed |
| | As IL | No reaction was observed |
|  | $[BMIm]^+$ | No reaction was observed |
| | As IL | No reaction was observed |

The results from epoxidation of GMO to EGMS, with two different catalysts were summarized in Table 4-3.

Four different ILs did not give any conversion of GMO, regardless of the catalyst had the same cation as the solvent or contained the $[BMIm]^+$ cation. Three of them were the same ILs that did not give any conversion of DAGMO, but also the piperidinium based IL failed to give any conversion of GMO. This could be due to the formation of a heterogeneous reaction system, giving lower reaction rates.

The most promising IL, when looking at the miscibility properties, was the phosphonium based IL. This, however, only resulted in the formation of

DHGMS. There was no sign at all of the desired EGMS. This was regardless of the cation in the catalyst. This IL was tested again, with the first sample taken after 5 minutes. DHGMS was already a problem here. The IL was also tested in enzymatic epoxidation by another in the project, but mostly hydrolysis was observed. This IL can therefore not be used as solvent for the epoxidation of GMO. The reason for the fast reaction compared to the other ILs tested could be the homogeneous reaction conditions, compared to a heterogeneous system with the other ILs.

Looking at the two functionalized imidazolium based ILs, the result was almost equal. Some conversion was observed, but not in sufficient amount. Hydrolysis and the formation of DHGMS was a problem. [BMIm][$Tf_2N$] showed surprisingly good conversion, although still far as good as the result for DAGMO.

On the basis of these results, it was decided to move on with the [BMIm][$Tf_2N$] IL.

The miscibilities for the substrates in this IL were therefore determined. This was done by mixing the substrate and IL in a 1:1 volume ratio before submitting the IL to NMR analysis, to see how much of the substrate has been dissolved in the IL. The result is seen in Table 4-4. The miscibilites were measured as molar ratios and weight ratios, for instance, 6.7 mol GMO was dissolved in 1 mol [BMIm][$Tf_2N$] corresponding to 0.14 g GMO/g [BMIm][$Tf_2N$].

**Table 4-4: Miscibilities of the substrates in [BMIm][$Tf_2N$]. The substrate and IL was mixed in a volume 1:1 ratio before sampling.**

| Substrate | GMO | EGMS | MHGMS | DHGMS | SNS |
|---|---|---|---|---|---|
| **Molar ratio** | 1 : 6.7 | 1 : 2.9 | 1 : 8.4 | 1 : 14.2 | miscible |
| **weight ratio** | 1 : 0.14 | 1 : 0.33 | 1 : 0.11 | 1 : 0.07 | |

This indicated that some of the EGMS will be present in the IL after reaction and it would be better to separate after hydrogenation as well. These results are consistent with the result from COSMO calculations performed by co-workers at Aarhus University.

## 4.4 Characterization of the $[BMIm]_3PW_{12}O_{40}$ catalyst

The mostly used catalyst $[BMIm]_3PW_{12}O_4$ has been characterized. Identification methods consisted of nuclear magnetic resonance (NMR) studies,, elementary analysis and infrared (IR) spectrometry.

NMR studies were made to measure the molar ratio between imidazolium and HPA. Two different batches of the catalyst were analyzed. Measurements were done by adding an internal standard (triisobutylphosphate) to the sample and both $^{1}H$ and $^{31}P$ NMR analysis was done. The integrals of the two spectra could be compared due to the internal standard. The ratio was calculated to 1:2.98 and 1:3.14 which was close to the theoretical value of 1:3.

Elementary analysis for C, H and N was also performed on two different batches of the catalyst and both were tested twice. The result is shown in Table 4-5. It can be concluded that the experimental values were close to the theoretical ones. The elementary analysis was performed at Copenhagen University.

**Table 4-5: Results of elementary analysis of the $[BMIm]_3PW_{12}O_{40}$ catalyst.**

| | C | H | N |
|---|---|---|---|
| **Theoretical values** | 8.75 | 1.38 | 2.55 |
| **Batch 1, sample 1** | 8.85 | 1.04 | 2.49 |
| **Batch 1, sample 2** | 8.83 | 0.98 | 2.46 |
| **Batch 2, sample 1** | 8.83 | 0.99 | 2.47 |
| **Batch 2, sample 2** | 8.87 | 1.02 | 2.49 |

In IR spectrometry it was possible to detect close association between imidazolium and HPA, this indicates a bond being present between imidazolium and HPA and the desired reaction between then has occurred. This work was done by a colleague at DTU.[106]

In IR spectrometry it was possible to detect close association between imidazolium and HPA, this indicates that the desired reaction between then has occurred. This work was done by a colleague at DTU[106] by exposing the

catalyst for $D_2O$ at 120 °C described by Kunov-Kruse and Thomsen[107] and very similar to the work by Jeon *et al*.[108] The result is displayed in Figure 4-7. The band around 3150 $cm^{-1}$ was the C2-H stretch for a weakly coordinated anion like HPA. For the starting material, [BMIm]Cl, the stronger coordinated anion was observed at 3050 $cm^{-1}$. This band was not observed in the spectrum for the catalyst, indicating no [BMIm]Cl was still present.

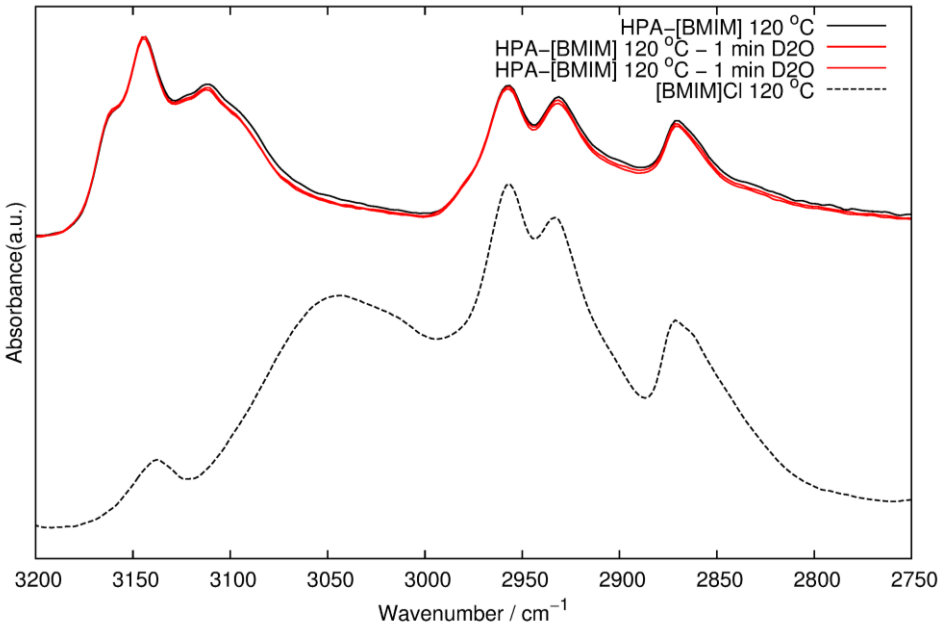



**Figure 4-7: Result of the IR spectrometry of $[BMIm]_3PW_{12}O_{40}$ after $D_2O$ exposure at 120 °C. HPA refers to $PW_{12}O_{40}^{3-}$.**[106]

Al this indicates that the prepared catalysts could be identified to be $[BMIm]_3PW_{12}O_{40}$ as wanted.

## 4.5 Epoxidation of glycerol monooleate in [BMIm][$Tf_2N$]

Different parameters were tested to look at the system with [BMIm][$Tf_2N$] as solvent, GMO as substrate, $[BMIm]_3PW_{12}O_{40}$ as catalyst and $H_2O_2$ as the oxidant. These include: stoichiometry of $H_2O_2$ addition, how the $H_2O_2$ was added, with or without air bubbling, stirring conditions, catalyst amount and how the catalyst was prepared.

Every time a new batch of catalyst was used, epoxidation of DAGMO was tested, to be sure of having an active catalyst.

Different amounts of $H_2O_2$ were tested to find the optimum. The following equivalents of $H_2O_2$ were tested compared to the GMO used. 1.1 eq, 1.5 eq, 2 eq, 3 eq and 5 eq. Adding 2, 3 or 5 eq $H_2O_2$ at once made the reaction mixture solid. These two experiments were therefore repeated with addition over time before any conclusion could be made. Addition of too much $H_2O_2$ caused the ringopening with water to DHGMS to take over, and conversion to DHGMS was therefore higher than conversion to EGMS. Adding too little will make the reaction go too slow and formation of DHGMS was a problem. From these experiments, it was concluded that 1.5 eq $H_2O_2$ compared to GMO was the best.

Addition of $H_2O_2$ could be done all at once or using an automatic burette dosimat to control the rate of addition. Just like with epoxidation of DAGMO, it improved the epoxidation reaction to have the $H_2O_2$ being added over time. Experiments with different equivalents and addition times were tested. Addition was tested over 0.5 hour, 1 hour and 3 hours. Also addition with half of the hydrogen peroxide over 1 hour, then 1 hour wait and then addition of the second half of hydrogen peroxide was tested. From these experiments, 1.5 eq $H_2O_2$ over 1 hour gave the best results. Addition of 2 eq with the same rate as 1.5 eq did not improve the reaction.

Air bubbling improved the epoxidation of DAGMO. It was therefore also tested in the epoxidation of GMO, but this was not beneficial, as more DHGMS than EGMS was formed. Lowering the reaction temperature to 50 °C decreased the amount of EGMS formed, but also decreased the formation of DHGMS. The

conversion to EGMS was however too slow and it was concluded that 50 °C was too low. 80 °C was also tested, but this was too high a temperature as hydrogen peroxide was degraded to fast.

Table 4-6 gives on overview of the initial tested parameters in the epoxidation of GMO.

**Table 4-6: Overview of initial testing of the epoxidation method.**

| Tested parameter | Reaction conditions | Conclusion |
|---|---|---|
| Amount of $H_2O_2$ | 1.1 eq, 1.5 eq, 2 eq, 3 eq and 5 eq | 1.5 equivalents was best |
| Addition time | 0.5 hour, 1 hour and 3 hours | Addition of 1.5 equivalents over 1 hour was best |
| Air bubbling | With or without air bubbling | Air bubbling was not beneficial |

The best result obtained at this point was 67 % conversion to EGMS, with 16 % GMO left and 17 % hydrolysis. There was no sign of DHGMS. This result was obtained by mixing 9 mL GMO, 30 mL [BMIm][$Tf_2N$] and 0.003 eq $[BMIm]_3PW_{12}O_{40}$ which were mixed and heated to 60 °C before 1.5 eq $H_2O_2$ was added over 1 hour. A GC sample was taken after 5 hours. A sample taken the next day shows that hydrolysis becomes a problem with too long reaction time. Unfortunately, when repeating this experiment, the same good result was not obtained.

Too see if an impurity from washing of the flask was the reason for the good result described above, the surfactant methyltrialkylammonium chloride ($C_8$-$C_{10}$) was added. This did not improve the epoxidation reaction.

Controlling the stirring was also tested. Too slow stirring improved the formation of DHGMS, but slows the hydrolysis. Too heavy stirring also improved formation of DHGMS. The optimum seems 250 RPM.

It was tested if the catalyst was better dispensed in the IL helped reaction. This was tested by a high shear mixer (homogenizer), where the catalyst and IL was thoroughly mixed. This was also tested with DAGMO as substrate. For both substrates the conclusion was that this did not help.

Adding a stronger solution of hydrogen peroxide (50 % compared to 36 % earlier) did not make any difference on the reaction. Another way of trying to remove the water from the reaction mixture was to apply vacuum to the system. This only increased the ring-opening of the epoxide to the dihydroxylated product.

Adding more catalyst improves the epoxidation, but does not increase the ring-opening to DHGMS. Adding less slows both reactions. Addition of 10 times the amount (0.03 eq) improved the reaction and a good result was obtained. After 3 hours the conversion to EGMS was 43 %, while 46 % was unconverted, 7 % was hydrolysed to free fatty acids and the amount of DHGMS was 4 %. After 80 hours the conversion to EGMS was 70 %, 8 % unconverted GMO, 9 % hydrolysis and 11 % DHGMS.

The preparation method for the $[BMIm]^+$ based catalyst was also investigated. The catalysts were evaluated by epoxidation of GMO and DAGMO. Two different preparation methods were evaluated, either adding all the [BMIm]Cl solution at once or by slow addition. It was slightly better to add the IL slowly, but there was no significant difference. The work up of the catalyst was tested by three different methods. The first method was no further purification than filtration and washing with water. The second method was dissolving the catalyst in acetone and removing the solvent *in vacuo* and the third batch was like the second, but with acetonitrile as solvent. The main difference between the two purification methods was that acetonitrile forms an azeotrope with water and acetone does not. Acetonitrile should therefore be better at removing the water from the catalyst. The best method was clearly the last, properly because of the better removal of water. Acetone treatment was still better than no work up. Several acetonitrile treatments further improved the result.

To further investigate the catalyst preparation, three different grinding methods were tested, either no grinding, using a mortar or wet ball mill

grinding. Grinding in a mortar or by wet ball mill gave almost the same particle size, namely 2180 Å and 1937 Å respectively. The catalyst without any further grinding had a particle size of 3064 Å. Testing with GMO as the substrate, the three catalysts gave the same results, whereas with DAGMO the best catalyst was the one without grinding. The two different grinding methods did not give any significant difference. It was not expected that the catalyst without grinding performed best as smaller particle size was expected to give a higher surface area. This would have given easier access to catalytic sites and thereby increasing the reaction rate.

Table 4-7 gives on overview of the initial tested parameters in the epoxidation of GMO.

**Table 4-7: Overview of the testing of the epoxidation method.**

| Tested parameter | Reaction conditions | Conclusion |
|---|---|---|
| Addition of surfactant | methyltrialkylammonium chloride ($C_8$-$C_{10}$) | This did not improve the epoxidation reaction. |
| Controlled stirring | Different stirring speeds were tested and high shear mixing | 250 RPM gave the best result. |
| Water content | A stronger $H_2O_2$ solution was added or removal of water by vacuum | This did not improve the epoxidation reaction. |
| Catalyst amount | 0.003 eq and 0.03 eq | Addition of more catalyst improved the epoxidation reaction, yielding the best result obtained. |
| Preparation method for the catalyst | The washing after formation of the catalyst was tested along with different grinding methods | The best result was washing with acetonitrile and no grinding. |

## 4.6 Preparation and test of an iron based catalyst

Because it was difficult to reproduce the good results with the previously described system, it was suggested to have a look at another catalyst. In 2012 dos Santos *et al* published the use of an iron based catalyst in [BMIm][$Tf_2N$] for the epoxidation of methyl oleate (MOA). The oxidant was either air or hydrogen peroxide. The best results was obtained using 15 bar air at 90 °C.[109] The structure of the catalyst is shown in Figure 4-8.

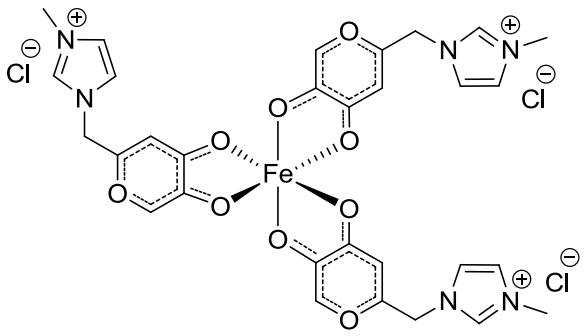



**Figure 4-8: Chemical structure of an iron based catalyst for epoxidation. Adapted from dos Santos *et al*.**[109]

The catalyst was prepared twice following the procedure described by dos Santos *et al*.[109] Kojic acid was treated with thionoyl chloride before substitution with *N*-methylimidazolium to give the imidazolium substituted intermediate (see Figure 4-9).

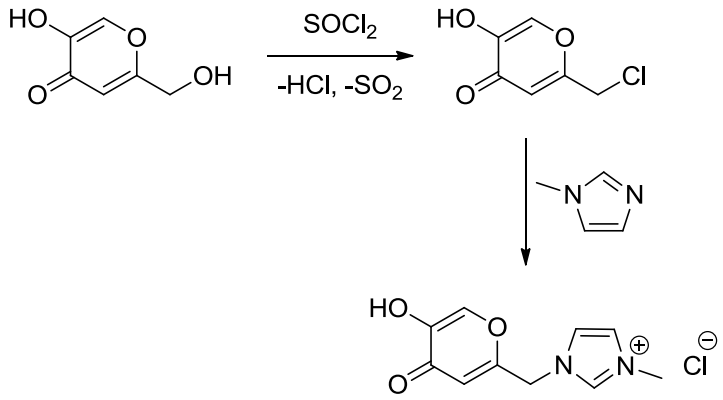



**Figure 4-9: Reaction scheme showing the formation of the imidazolium substituted intermediate for the iron based catalyst. Adapted from dos Santos *et al*.**[109]

Treatment of 3 equivalents of the imidazolium substituted intermediate with iron(III)chloride resulted in the desired catalyst, see Figure 4-10.

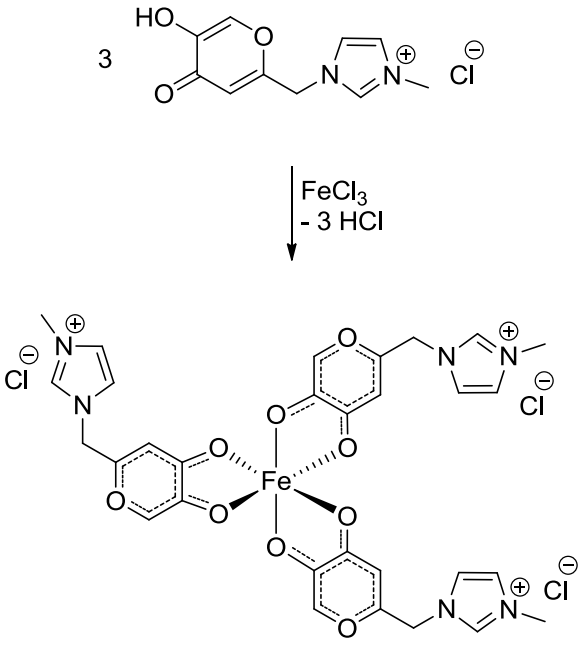



**Figure 4-10: Reaction scheme showing the formation of the iron based catalyst from $FeCl_3$ and three equivalents of the imidazolium substituted intermediate. Adapted from dos Santos *et al*.**[109]

Three different scenarios were tested: simple air bubbling through the system (1 bar), experiments in an autoclave (15 bar) and epoxidation with hydrogen peroxide as the oxidant.

The epoxidation with hydrogen peroxide was tested on GMO and DAGMO at 60 °C. The reaction temperature was lower than using air as oxidant, because hydrogen peroxide is decomposing at higher temperatures, but higher than the reported epoxidation temperature because our previous results showed no epoxodation of neither GMO or DAGMO at too low temperature. Unfortunatly, both epoxidations were unsuccessful and no conversion was observed.

Air bubbling was tested as an epoxidation method for GMO, DAGMO and MOA. Reaction temperature was 90 °C and air bubbled through with a rate of 15 L/minute. Neither compounds gave any conversion to the epoxides. Looking at the publication from dos Santos *et al*, even though they describe air bubbling as a method, it was not expected to give much conversion.

Experiments at higher pressures of air were performed with GMO, DAGMO and MOA in an autoclave. All experiments were done with 15 bar and 90 °C as this was reported to be the optimum. For GMO and DAGMO, both the suggested iron containing catalyst and the HPA-based catalysts were tested. Unfortunately all experiments with GMO and DAGMO failed to give any conversion. For MOA, a conversion was observed after 24 hours of reaction time, although still starting material left in the reaction mixture. The product formed was not validated to be the epoxide, as a mistake occurred when analyzing on GC-MS.

# Chapter 5
# Epoxidations with peracetic acid

Since the catalytic epoxidation reactions described in Chapter 4 did not give the desired results, epoxidation using peracetic acid was tested instead. The epoxidation using peracids is known as the Prileszhaev (or Prileschajew) reaction and was first described in 1909 with the use of perbenzoic acid[110] Peracetic acid is a stronger oxidant than hydrogen peroxide and often no catalyst is needed to initiate the reaction and milder reaction conditions are often applied.[111] Epoxidation of vegetable oils on industrial scale are often performed with peracetic- or performic acid with high conversions.[112] It is important to note that epoxidation using peracetic acid is highly exothermic and heat transfer is an important issue when running the reaction. Addition of peracetic acid is therefore often done over a relative long period.[111,113]

Peracetic acid can be added preformed or generated *in situ*. The generation of peracetic acid *in situ* is done from acetic acid and hydrogen peroxide. An acid catalyst is required for this process; often a mineral acid like sulfuric acid is used, see Figure 5-1. The rate determining step is the formation of the peracetic acid.[111,113] The *in situ* method is generally considered safer, because of lower concentrations of the highly oxidative peracetic acid.[113,114] This system forms two phases with the unsaturated oil, with the peracid transferred from the aqueous phase, where it is generated, to the organic phase, to react with the oil.[114]

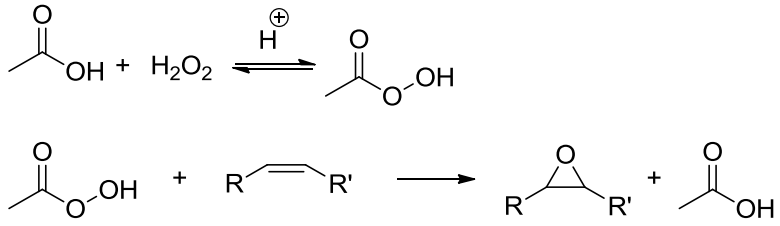


**Figure 5-1: Epoxidation with peracetic acid generated *in situ* can be divided into two reactions.**

When the peracid is reacted with the olefin, the parent carboxylic acid is formed. The mechanism for the Prilezhaev reaction is known as the "butterfly mechanism".[115,116]

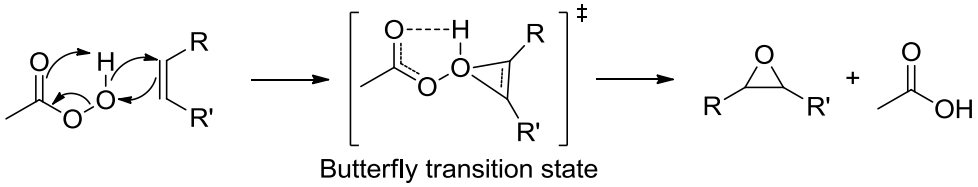



**Figure 5-2: Proposed mechanism for the Prilezhaev reaction, known as the "butterfly mechanism". Adapted from Laue and Plagens.**[115]

Studies have shown that the Prileszhaev reaction provides *syn* addition, meaning that the stereochemical relations of the substituents in the alkene are retained after the reaction.[115]

Previous experiments at Dansico A/S have shown that *in situ* formation of peracetic acid for epoxidation causes hydrolysis, probably due to the acidic catalyst. Epoxidation with *meta*-chloroperoxybenzoic acid (*m*-CPBA) in chloroform on the other hand has proven to be efficient, but because of the waste product (*meta*-chlorobenzoic acid) this was not the desired way to form the epoxide. Also the use of chloroform was not desired because of the high price and low sustainability.[72]

Epoxidation of GMO with peracetic acid has previously been described by Schiemann and Schneider in 1967. Epoxidation in acetic acid at 25 °C gave 87 % epoxide after 4 hours.[117] Also the epoxidation of DAGMO with the use of peracetic acid in acetic acid has previously been described.[118]

Like the experiments described in the previous chapter, all results were obtained by analyzing samples on GC. In this chapter, ring-opening of the epoxidized compound could also be initiated by acetic acid to form a hydroxy-acetoxy compound, but this compound could not be separated from the dihydroxylated compound by the GC method applied. Referring to DHGMS in this work also covers the hydroxy-acetoxy analogue.

## 5.1 Initial experiments

Initially both DAGMO and GMO were tested in the epoxidation reaction with peracetic acid. The solvent used was either [BMIm][$Tf_2N$] or acetic acid. Acetic acid was tested as solvent as it is also formed in the reaction from peracetic acid. Furthermore, acetic acid should also be added in the final step, in the process, the acetylation reaction, and it was therefore not seen as an extra solvent. Solvent amount added was the same as used in the previous chapter, 30 mL solvent to 9 mL GMO or 11 mL DAGMO. Catalysts tested were both catalyst described in the previous chapter: the [BMIm] substituted HPA based catalyst or the iron based catalyst, both added in 0.003 equivalents. Reactions were performed at 60 °C with addition of peracetic acid (1.1 eq) at once. Experiments with acetic acid as solvent looked very promising, but 3 hours were already too long reaction time. Looking at the results for GMO, hydrolysis was the major problem, already after 3 hours, but also the formation of a dihydroxylated product was a problem. With DAGMO as the substrate some hydrolysis was also observed, especially with IL as solvent, but using acetic acid as solvent was better. Still, after 3 hours, some unconverted starting material was observed with both substrates, though not much.

The next experiments were performed only with acetic acid as the solvent and still testing both DAGMO and GMO. Catalysts were the ones mentioned above or without any catalyst, because of the high reactivity of peracetic acid.[111] Reaction setup and conditions were the same as before, but with shorter

reaction time. Results for GMO showed that the experiments without a catalyst looked very promising, although hydrolysis was still a major problem. Also the formation of DHGMS was a problem. For DAGMO, the conversion to the epoxide was high after 15 minutes even with no catalyst present. Also for DAGMO, the ring-opening to the dihydroxylated product was a problem.

Because of the formation of the dihydroxylated product for both substrates was a problem and also hydrolysis of GMO, two different scenarios were tested. Firstly adding acetic anhydride to the reaction to remove the water present in the peracetic acid, secondly lowering of the temperature to 30 °C was also tested. The amount of acetic anhydride was calculated after measuring the water content of the peracetic acid by a Karl-Fischer titration. The result was 14.3 % water.

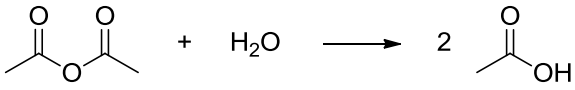



**Figure 5-3: Addition of acetic anhydride can remove water by formation of acetic acid.**

Both scenarios were tested with both substrates, without catalyst and with acetic acid as the solvent, as this were the most promising reaction conditions. The reactions were performed like previously described, everything was mixed except peracetic acid, the mixtures where then heated to the desired temperature before the addition of peracetic acid. With the addition of acetic anhydride less of the dihydroxylated product was observed for DAGMO (9 % after 30 minutes), but it was still an issue for GMO (35 % after 30 minutes). Dihydroxylation was however also observed for DAGMO at longer reaction time (72 % after 3 hours). The hydrolysis of GMO decreased after the addition of acetic anhydride. Lowering the temperature was very promising. For DAGMO, a conversion to EDAGMS of 92 % was already observed after 30 minutes, dihydroxylation or hydrolysis was not observed. For GMO the result was also very promising. After 30 minutes almost all GMO was converted to EGMS. Neither hydrolysis nor dihydroxylation were an issue. The conversions were 76 % EGMS, 7 % free fatty acids (from hydrolysis) and 5 % DHGMS. 12 % of GMO was unconverted after 30 minutes.

Because of previous problems with reproducing good results in the epoxidation reaction with GMO, a second experiment with the same reaction conditions was performed. This time it was possible to reproduce the result, giving 79 % EGMS, 11 % free fatty acids, 10 % unconverted starting material. The dihydroxylated product was not observed. Further work was therefore only conducted only with GMO as the substrate and not with DAGMO, as this was not the desired substrate for the process.

For the small scale system with 9 mL GMO, different amounts of acetic acid as solvent were tested. 15 mL, 7.5 mL and no solvent was tested. The result for this was that hydrolysis was increased when less solvent was added. This must be because the epoxidation is an exothermic reaction and with less solvent, it was harder to remove the heat and a higher temperature was therefore obtained, increasing the risk of hydrolysis.

**Table 5-1: Overview of the initial testing of the epoxidation method by peracetic acid.**

| Tested parameter | Reaction conditions | Conclusion |
|---|---|---|
| Solvent tested | [BMIm][$Tf_2$] or acetic acid; both DAGMO and GMO was tested | Using acetic acid was the best solvent |
| Catalyst tested | $[BMIm]_3PW_{12}O_{40}$, iron(III) complex and no catalyst, both DAGMO and GMO was tested. | No catalyst gave the best result gave the best result. |
| Lower formation of byproducts | Acetic anhydride was added or the temperature was lowered | Addition of acetic anhydride resulted in decreased ringopening of EDAGMS but had no effect on EGMS. Lowering the temperature decreased the formation of by-products |
| Amount of acetic acid | To 9 mL GMO: 30 mL, 15 mL and 7.5 mL | Decreasing the amount of solvent increased the hydrolysis of the glycerol backbone. |

5 times up scaling of the reaction was tested. The addition of peracetic acid was done over 3 minutes instead of addition at once as for the smaller reactions. This was done because of increasing temperature in the reaction mixture. The reaction temperature increased 9 °C during the addition of peracetic acid. After 30 minutes a good conversion to EGMS was observed and after 1 hour of reaction time, almost no GMO was present. The result after 1 hour was 80 % EGMS, 13 % hydrolyzed product and 7 % unconverted GMO. The higher amount of hydrolysis must be due to the higher temperature increase compared to small scale reactions.

## 5.2 Storage of EGMS

A sample from the upscaling experiment was taken after 24 hours. The sample analysis showed that all of EGMS had decomposed after the long reaction time. It was therefore investigated how EGMS could be stored. A new batch of EGMS was prepared as described above and after taking a sample, the reaction mixture was stored at -18 °C. The reaction mixture was frozen the next day. A sample was taken and analyzed, showing EGMS was still the main component of the mixture with 79 % EGMS after 72 hours at -18 °C compared to 85 % before storage. This was also observed the following days. Unfortunately when liquefying the sample, EGMS had decomposed during this process. It was therefore concluded that EGMS should be transferred directly to the hydrogenation step as it was not possible to store the epoxide.

## 5.3 Optimization of the temperature

The following experiments were an 11 times up scaling of the original experiments. This means 99 mL GMO was used. The first experiment was with the same reaction conditions as the small scale experiments, though addition of peracetic acid was done over 25 minutes. After 1 hour the conversion to EGMS was 76 %, 6 % DHGMS was observed along with 8 % hydrolysis and 9 % unconverted GMO.

Different reaction temperatures were also investigated. The reaction was tested at 10 °C, 20 °C and 40 °C. Reaction performed at RT was also tested. Furthermore, experiments with adding peracetic acid at 20 °C and then

keeping the temperature at the resulting temperature after addition, which was 35 °C. 10 °C was too low a temperature because the conversion was very slow and the reaction mixture became unclear because the mixture of GMO in acetic acid was close to the melting point. 20 °C resulted in a longer reaction time than 30 °C, almost the same amount of by-products combined were observed. After 2.5 hours the conversion to EGMS was 77 %, unconverted GMO was 7 %, hydrolysis was 11 % and ring-opening was 5 %. When starting addition at 20 °C and then keeping the temperature at the resulting temperature gave a good result. After 2 hours 78 % EGMS was observed along with only 1 % unconverted GMO, 7 % ring-opening and 13 % hydrolysis. At RT, an ok result was observed, even though there were some problems when adding the peracetic acid. After 2 hours 77 % was converted to EGMS, 2 % was left unconverted, 12 % hydrolysis was observed and 10 % ring-opening. The high amount of by-products must be due to the high temperature obtained when addition of peracetic acid was too fast. 40 °C gave a lot of hydrolysis, but reaction time was short. After 1 hour conversion to EGMS was 84 % and only 2 % unconverted material was observed. 12 % hydrolysis and 2 % ring-opening was observed.

From these experiments, it was concluded that 30 °C provided the best results and this temperature was used for the investigations on rate of addition of peracetic acid, stoichiometry of peracetic acid and solvent amount. When these parameters had been optimized, further investigations were performed looking at the temperature. A system with 10 times the volume ratio of solvent and 1.1 equivalents of peracetic acid was tested at 20 °C, 25 °C and 30 °C. After 1 hour at 30 °C a 86 % conversion to EGMS was observed. Unconverted GMO was analyzed to be 10 %. The rest were by-products from hydrolysis and ring-opening. The amount of EGMS was hereafter stable around 86 %, whereas the amount of GMO decreased and the amount of byproducts were increased. Running the experiment at 20 °C resulted in longer reaction times. It was not until after 1 hour and 45 minutes that the conversion to EGMS reached a maximum at 70 %. Hydrolysis and ring-opening was no longer observed at this reaction temperature, but there was a large amount of unconverted GMO. Running the experiment at 25 °C seemed optimal. After 2.5 hours only 12 % GMO was left in the reaction mixture, 1 % hydrolysis and 7 % ring-opening. The conversion to EGMS was 80 %. After 5 hours, no GMO was left in the reaction

mixture and the amount of EGMS was 87 %. At this point an increased amount of DHGMS (10 %) and hydrolysis (2 %) was observed.

The final conclusion on the reaction temperature was 25 °C to be the optimum. Another advantage of this, compared to the first conclusion of 30 °C.

## 5.4 Optimization of the amount of peracetic acid

Optimization of the amount of peracetic acid was performed with the system containing 99 mL GMO and 330 mL acetic acid. The different amounts of peracetic acid tested for this system were 1.01 eq, 1.1 eq and 1.5 equivalents. 1.01 equivalents was clearly too little, as the conversion to EGMS was too slow and the hydrolysis and formation of the dihydroxylated product became significant compared to the conversion to EGMS. Comparing the addition of 1.1 and 1.5 equivalents, it can be concluded that 1.5 equivalents ensure faster formation of the desired EGMS, but also formation of the by-products.

For these experiments, it was concluded that 1.1 equivalents of peracetic acid compared to GMO gave the best results.

## 5.5 Optimization of the rate of the addition of peracetic acid

The reaction is exothermic and a slow addition of peracetic acid was therefore important. Too fast addition increases the maximum temperature obtained in the reaction mixture, resulting in formation of DHGMS. Reactions with controlled addition of peracetic acid were first performed on a model system with 99 mL GMO and 330 mL acetic acid. First the addition of 1.1 equivalents at a rate of 2.5 mL/minute (resulting in an addition time of approximately 23 minutes) was tested. This looked very promising. Addition of the same amount of peracetic acid at 5 mL/minute resulted in more ring-opening and hydrolysis. It was also tested to add the peracetic acid with an increasing addition rates over approximately 23 minutes, this did not improve the conversion. Transferring the addition over 23 minutes to smaller or larger scaled systems gave the same result. The addition of 1.5 eq. peracetic acid at the same rate

(2.5 mL/minute) also looked promising, but the best results were achieved by the addition over approximately 23 minutes.

The conclusion was that the addition of peracetic acid should take approximately 23 minutes. Both faster and slower addition resulted in higher formation of the by-products.

## 5.6 Optimization of the amount of solvent

Different amounts of acetic acid as solvent were tested, both in small scale (9 mL GMO) and larger scale (99 mL GMO). Small scale experiments showed that less solvent than the firstly used (GMO to acetic acid was 0.3:1 (volume based)) resulted in higher conversion to the two by-products: free fatty acids from hydrolysis or ring-opening to DHGMS. The largest scale where the ratio between solvent and GMO was tested was with 99 mL GMO. Several experiments were conducted, only varying the solvent amount.

It can be concluded that adding less solvent increased the formation of by-products . Addition of too much solvent is a cost issue. From these experiments, a volume ratio of 1:10 for GMO in acetic acid was the best accepted (99 mL GMO to 990 mL acetic acid). In this calculation, the amount of acetic acid added or formed with the peracetic acid is not taken into account. This ratio is also the ratio applied in the acetylation reaction, as tested by another in the project.

## 5.7 Effect of water content and sulfuric acid present

Too see the effect of the peracetic acid concentration, a mixture of peracetic acid, water and acetic acid was made, to reduce the peracetic concentration with 50 %, but still with 14 % water present. This way, the amount of water was higher than previous experiments. Reaction temperature was 30 °C. After 2 hours the amount of EGMS was only 67 %. This was due to high amount of by-products: hydrolysis was 16 % and ring-opening was 12 %. Only 3 % GMO was left unconverted. The higher water amount thereby increases hydrolysis and ring-opening, though this was not surprising.

One difference between preformed peracetic acid and *in situ* formation of peracetic acid is the presence of an acid catalyst in the *in situ* formation. The system was therefore tested with addition of sulfuric acid to see the effect of sulfuric acid. The result was still a good conversion to EGMS, but hydrolysis was a larger problem here than previous, 15 % compared to a maximum of 13 % without sulfuric acid present. It can therefore be concluded that the system with addition of preformed peracetic acid was the best.

## 5.8 Experiments in larger scale

For the experiments in larger scale, 180 mL GMO and 1.8 L acetic acid was used, retaining the ratio as described above. The reaction temperature was 25 °C, also as described above. Four different amounts of peracetic acid were tested, namely 1.1 eq, 1.5 eq, 2 eq and 5 equivalents. In all experiments, the peracetic acid was added over approximately 23 minutes with an automatic burette dosimat. Adding 5 equivalents were too much, more DHGMS than EGMS was observed. This was not surprising as more water was also added this way.

For the addition of 1.1 equivalents, the conversion as a function of time is displayed in Figure 5-4. After 3 hours, 82 % EGMS was observed and 10 % unconverted GMO. Only small amounts of the by-products were formed.

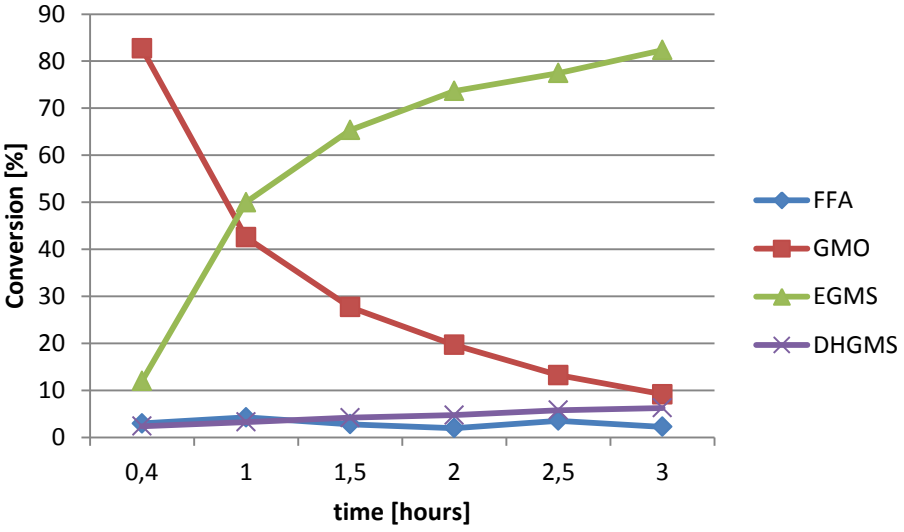



**Figure 5-4: Conversion as a function of time for the addition of 1.1 equivalents of peracetic acid. Reaction conditions: 180 mL GMO and 1.8 L acetic acid was heated to 25 °C before peracetic acid (1.1 eq.) was added with 4.69 mL/minute.**

Adding 1.5 equivalents peracetic acid gave a really good result. The conversion as a function of time can be seen in Figure 5-5. After 2.5 hours the amount of GMO was so small, it could not be integrated when analyzing the results from GC. After 4 hours no GMO was left. After 3 hours, the conversion to EGMS was 87 %, unfortunately also 9 % DHGMS was observed.

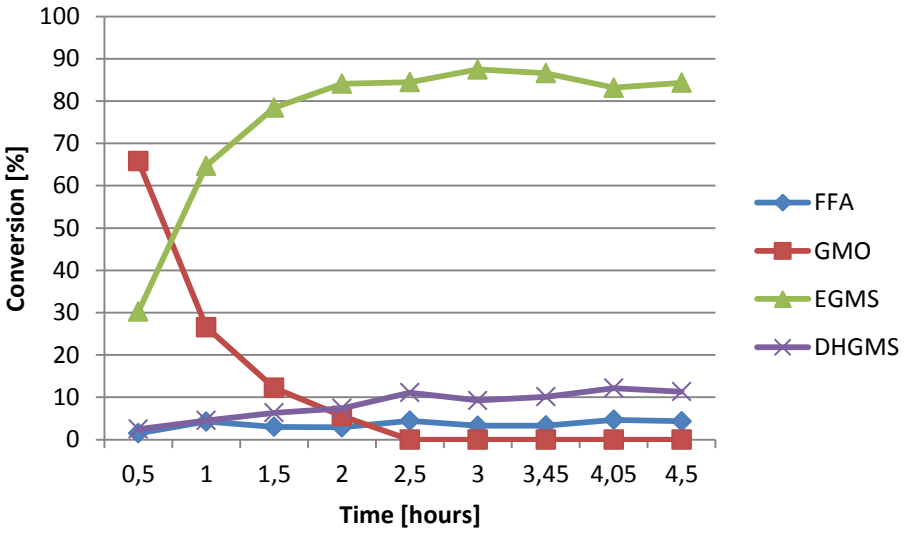



**Figure 5-5: Conversion as a function of time for the addition of 1.5 equivalents of peracetic acid. Reaction conditions: 180 mL GMO and 1.8 L acetic acid was heated to 25 °C before peracetic acid (1.5 eq.) was added with 9.15 mL/minute.**

For the addition of 2 equivalents of peracetic acid, the result is displayed in Figure 5-6 as conversion as a function of time. After 2.5 hours no GMO was left in the reaction mixture, though the amount of by-products were higher than with smaller amounts of peracetic acid.

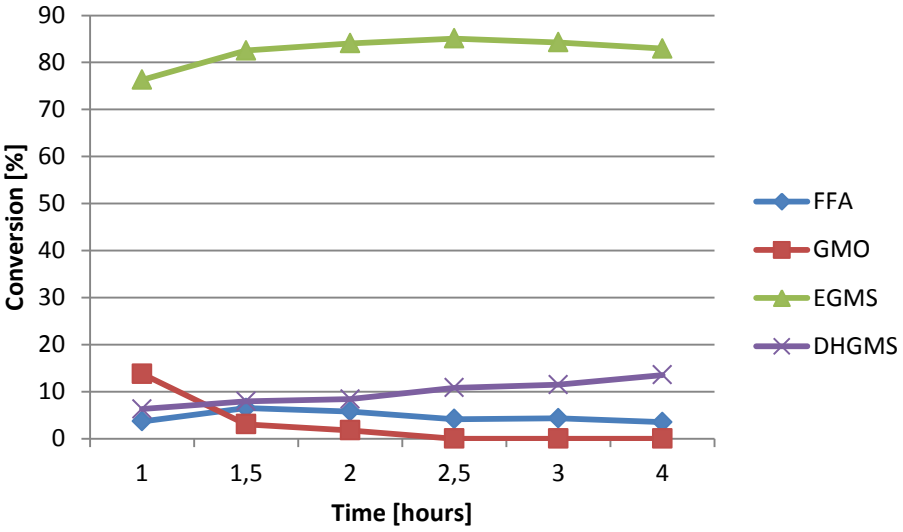



**Figure 5-6: Conversion as a function of time for the addition of 2 equivalents of peracetic acid. Reaction conditions: 180 mL GMO and 1.8 L acetic acid was heated to 25 °C before peracetic acid (2 eq.) was added eith 2.5 mL/minute.**

By comparing Figure 5-4, Figure 5-5 and Figure 5-6 the task was to find the best acceptable ratio between reaction time and tolerated amount of byproducts. It was concluded that 1.5 equivalents was the best solution.

## 5.9 Final remarks

From all of the above experiments, the optimum epoxidation conditions were as follows: 180 mL GMO and 1.8 L acetic acid were mixed and heated to 25 °C. 1.5 eq peracetic acid (137 mL) were added over approximately 23 minutes. After 3 hours, all GMO was converted and the reaction mixture can be transferred to an autoclave for hydrogenation.

Due to the exothermic nature of this reaction, the heat of reaction is to be measured using a calorimeter, before further up-scaling of the reaction is performed.

# Chapter 6
# Catalytic transfer hydrogenation

The second step in the final suggested synthesis pathway is a reduction of the epoxide EGMS to the monohydroxy compound MHGMS. This reduction was tested by using a hydrogen donor to form hydrogen *in situ* in a catalytic transfer hydrogenation (CTH) or the more traditional way using hydrogen gas (see Chapter 7).

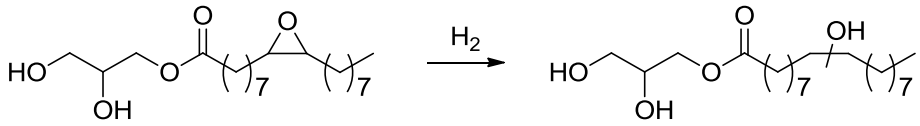



**Figure 6-1: Reductive opening of EGMS to either of the two monohydroxy compounds collectively known as MHGMS.**

The reduction or hydrogenation with either molecular hydrogen or a hydrogen donor is important in both industry and small scale laboratory work. CTH is considered a safer method to reduce compounds, as the use of molecular hydrogen is hazardous. Also CTH does not require any special pressure vessels, only simple stirring.[119]

The pioneering work of CTH was performed in the early 1950's by Linstead, Braude and coworkers.[120,121] Poor yields and long reaction times were described, causing this work to be ignored by many. Since then efforts have been made to investigate this way of reducing various compounds. Chemoselectivity can often be achieved by varying the catalyst, hydrogen donor or reaction conditions.[122] Although some work has been put into CTH, reductions using molecular hydrogen or a hydride donor is still mostly used.[119]

The best hydrogen donors have elements or groups with electronegativity comparable with hydrogen itself. This includes formic acid and formates.[119,123]

## 6.1 Examples of catalytic transfer hydrogenations

Catalytic transfer hydrogenation of epoxides to the corresponding mono-hydroxy compound with the use of $NH_4HCO_2$ has been described by Varghese *et al* in 1995. Different epoxides were tested, both terminal and internal, among them, cyclohexene oxide. The catalyst described was Pd/C and the solvent used was methanol. The reaction was performed at 45 °C for 18 hours, giving a 70 % yield.[124] Also Dragovich *et al* has described the opening of epoxides with $NH_4HCO_2$ in ethanol, though only for terminal alkenes.[125] If the epoxide is not symmetrical, two different mono-hydroxy compounds can be formed. Terminal epoxides are often reduced to the internal alcohol with $NH_4HCO_2$.[126]

For the use of $NH_4HCO_2$ as a hydrogen donor, the reaction displayed in Figure 6-2 occurs. Note that all products formed are gasses and the byproducts are therefore easy to remove.


**Figure 6-2: Reaction of $NH_4HCO_2$ as a hydrogen donor. All products are gasses.**

For the use of the azeotropic mixture HCOOH:$Et_3N$ 5:2 as donor, $Et_3N$ is not consumed during the reaction, but acts as a co-catalyst as displayed in Figure 6-3. Otherwise, only gaseous products are formed.

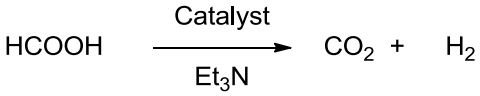



**Figure 6-3: Using HCOOH:$Et_3N$ 5:2 as a hydrogen donor results in two gaseous compounds, but besides the catalyst, also $Et_3N$ will have to be removed after reaction.**

ILs have been tested as solvent for this reaction.[127,128]

Alternatively, a basic IL can also be used as both solvent and co-catalyst. This has for instance been described for the reduction of aromatic ketones to alcohols.[129]

Using 2-propanol as the hydrogen donor will, unlike the two previous examples, result in a liquid by-product, namely acetone, which will have to be removed after the reaction. It was calculated that if 1 ton of final product (SNS-A) was to be produced by transfer hydrogenation with 2-propanol, approximately 120 kg of acetone would be produced. The reaction is displayed in Figure 6-4. Furthermore, the use of 2-propanol also needs a co-catalyst to release hydrogen, e.g. KOH[130] or HCl(aq).[131]

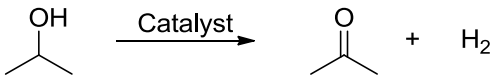



**Figure 6-4: Formation of acetone as a result of using 2-propanol as the hydrogen donor.**

CTH in ionic liquids was described by Baán *et al* in 2005 using $NH_4HCO_2$ as hydrogen donor.[132] The reaction was described using methyl cinnamate as substrate and [BMIm][$BF_4$] as solvent (see Figure 6-5).

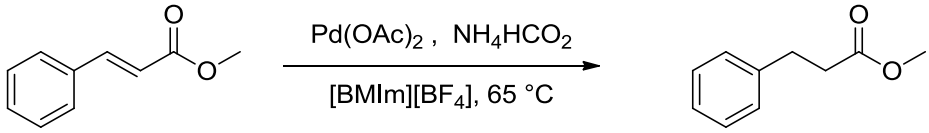



**Figure 6-5: Reduction of methyl cinnamate using $NH_4HCO_2$ as hydrogen donor. Adapted from Baán *et al*.**[132]

## 6.2 Model substrates

Three different model substrates were tested in the reduction using a hydrogen donor: cyclooctene oxide, cyclohexene oxide and methyl cinnamate. Three different hydrogen donors were tested: $NH_4HCO_2$, 2-propanol and a mixture of formic acid and triethylamine ($Et_3N$). Three different catalysts have been tested: $Pd(OAc)_2$, Pd/C and Ru/C.

As a test substrate for the CTH of on epoxide to a mono-hydroxy compound cyclooctene oxide was chosen:

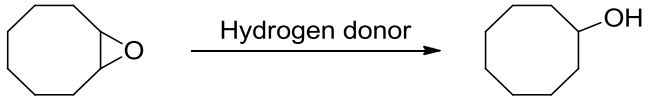



**Figure 6-6: Hydrogenaton of cyclooctene oxide to cyclooctanol using a hydrogen donor**

The first hydrogen donor tested was $NH_4HCO_2$. Reaction conditions can be seen in Table 6-1. Most experiments were performed with 3 equivalents of $NH_4HCO_2$ compared to cyclooctene oxide, but higher amounts (5 and 10 equivalents) were also tested. The amount of solvent was 2 mL to 0.5 mmol of cyclooctene oxide.

**Table 6-1: Overview of reaction conditions and results of the CTH of cyclooctene oxide with $NH_4HCO_2$ as donor, 3 equivalents if nothing else is specified. Solvent amount was 2 mL to 0.5 mmol substrate.**

| Solvent | Catalyst | Reaction conditions | Conclusion |
|---|---|---|---|
| [BMIm][$BF_4$] | $Pd(OAc)_2$ | 45 °C, 1 day or 3 days | No reaction |
| | | 65 °C 1 day or 3 day | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| | | 65 °C 1 day or 3 days | No reaction |
| | Ru/C | 45 °C, 1 day; | No reaction |
| | | 80 °C, 1 day | No reaction |
| | | 10 equivalents 80 °C, 1 day | No reaction |
| [BMIm][$Tf_2N$] | $Pd(OAc)_2$ | 45 °C, 1 day or 3 days | No reaction |
| | | 65 °C 1 day or 3 days | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| | | 65 °C 1 day or 3 days | No reaction |
| | Ru/C | 10 equivalents 50 °C, 1 day | No reaction |
| | | 10 equivalents 60 °C, 1 day | No reaction |

| Solvent | Catalyst | Reaction conditions | Conclusion |
|---|---|---|---|
| [EMIm][$Tf_2N$] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | | 65 °C 1 day or 3 days | No reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | | 65 °C 1 day or 3 days | No reaction |
| [EMIm][$EtOSO_3$] | $Pd(OAc)_2$ | 45 °C, 1 day or 3 days | No reaction |
| | | 65 °C 1 day or 3 days | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| | | 65 °C 1 day or 3 days | No reaction |
| Methanol | $Pd(OAc)_2$ | 45 °C, 1 day or 3 days | No reaction |
| | | 60 °C, 1 day | No reaction |
| | | 80 °C, 1 day or 3 days | No reaction |
| | | 5 equivalents 80 °C, 3 days | No reaction |
| | | 10 equivalents 60 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| | | 60 °C, 1 day | No reaction |
| | | 80 °C, 1 day or 3 days | No reaction |
| | | 5 equivalents 80 °C, 3 days | No reaction |
| | | 10 equivalents 60 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | | 80 °C, 1 day or 3 days | No reaction |
| | | 10 equivalents 60 °C, 1 day | No reaction |
| Ethanol | $Pd(OAc)_2$ | 45 °C, 1 day or 3 days | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| [BMIm][ $BF_4$] and methanol 1:1 | $Pd(OAc)_2$ | 80 °C, 1 day or 3 days | No reaction |
| | | 5 equivalents 80 °C, 3 days | No reaction |
| | Pd/C | 80 °C, 1 day or 3 days | No reaction |
| | | 5 equivalents 80 °C, 3 days | No reaction |
| | Ru/C | 80 °C, 1 day or 3 days | No reaction |
| [BMIm][ $Tf_2N$] and methanol 1:1 | Ru/C | 10 equivalents 50 °C, 1 day | No reaction |
| | | 10 equivalents 60 °C, 1 day | No reaction |

As displayed in Table 6-1, CTH of cyclooctene oxide with $NH_4HCO_2$ as hydrogen donor and various reaction conditions did not result in any conversions of cyclooctene oxide. This hydrogen donor was therefore abandoned for further investigations.

The use of HCOOH and $Et_3N$ as a hydrogen donor was only tested with [BMIm][$Tf_2N$] as the solvent. HCOOH:$Et_3N$ 5:2 can be added as a preformed complex (C) or added separately (A: ratio 5:2, B: ratio 5:5). The reaction conditions and results are displayed in Table 6-2. The amount of HCOOH was 5 equivalents. The solvent tested was [BMIm][$Tf_2N$] and the amount added was 1 mL to 0.5 mmol.

**Table 6-2: Overview of reaction conditions and results of using HCOOH:$Et_3N$ 5:2 as a hydrogen donor for the CTH of cyclooctene oxide. A: HCOOH and $Et_3N$ was added separately in a ratio of 5:2, B: HCOOH and $Et_3N$ was added separately in a ratio of 5:5, HCOOH:$Et_3N$ 5:2 was added as a preformed complex. The solvent amount was 1 mL to 0.5 mmol substrate.**

| Catalyst | HCOOH addition | Reaction conditions | Conclusion |
|---|---|---|---|
| $Pd(OAc)_2$ | Method A | 30 °C, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | Method B | 30 °C, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | Method C | RT, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | | no solvent, 60 °C, 1 day | No reaction |
| Pd/C | Method A | 60 °C, 1 day | No reaction |
| | Method B | 60 °C, 1 day | No reaction |
| | Method C | RT, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | | no solvent, 60 °C, 1 day | No reaction |
| Ru/C | Method A | 30 °C, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | Method B | 30 °C, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | Method C | RT, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | | no solvent, 60 °C, 1 day | No reaction |

As displayed in Table 6-2, the tested reactions conditions for using HCOOH:$Et_3N$ 5:2 as a hydrogen donor in the CTH of cyclooctene oxide all resulted in no conversion of the starting material. The use of formic acid as the

hydrogen donor was therefore abandoned for the use of CTH of cyclooctene oxide.

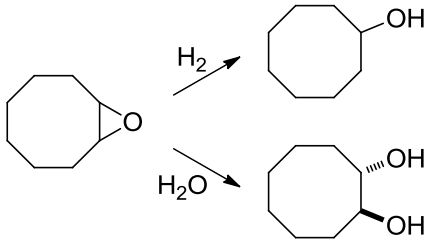
The use of 2-propanol as the hydrogen donor was tested in different solvents and with different catalysts and co-catalysts. This is displayed in Table 6-3. The amount of solvent was tested with both 1 mL and 1.5 mL to 0.5 mmol cyclooctene oxide. The amount of 2-propanol was 1.8 equivalents.

**Table 6-3: Overview of the initial reaction conditions and results of the CTH of cyclooctene oxide using 2-propanol as the hydrogen donor (1.8 equivalents). Amount of solvent was 1.5 mL to 0.5 mmol substrate.**

| Solvent | Catalysts | Reaction conditions | Reaction |
|---|---|---|---|
| [BMIm][$BF_4$] | Ru/C, KOH | 80 °C, 1 day | No reaction |
| | Ru/C, HCl(aq) | 80 °C, 1 day | Reaction to both cyclooctanol and 1,2-cyclooctadiol, slightly more of the diol. All starting material was converted. |
| [BMIm][$Tf_2N$] | Ru/C, KOH | 50 °C, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |
| | | 80 °C, 1 day | No reaction |
| | Ru/C, HCl(aq) | 80 °C, 1 day | Reaction to both cyclooctanol and 1,2-cyclooctadiol, slightly more of the diol. All starting material was converted. |
| - | Ru/C, KOH | 50 °C, 1 day | No reaction |
| | | 60 °C, 1 day | No reaction |

As displayed in Table 6-3 a reaction was observed with cyclooctene oxide when using 2-propanol and the acidic co-catalyst. Both ILs tested showed the same trend. Unfortunately, the main product was the by-product 1,2-cyclooctadiol.

This could be from ring-opening with the water present in the co-catalyst to the trans diol by a $S_N2$ mechanism.




**6-7: Conversion of cyclooctanol using 2-propanol, Ru/C and HCl(aq) as reactant resulted not only in the desired cyclooctanol, but also 1,2-cyclooctadiol, formed by reaction with water.**

Because of the first observed reaction with cyclooctene oxide when using 2-propanol and an acidic co-catalyst in either ILs tested at 80 °C, different amounts of 2-propanol and HCl(aq) were tested to see if it was possible to reduce the amount of by-product. For both ILs, 1.07 and 1.8 equivalents of 2-propanol were tested with the same amount of HCl(aq) as before or with twice the amount. Using less 2-propanol resulted in lower conversion, but problems with diol formation in equal amount as the mono-ol remained. It was difficult to see any effect of increased amounts of co-catalyst.

The conclusion of the CTH of cyclooctene oxide is that only 2-propanol gave a conversion under the reaction conditions tested. Unfortunately the water present in the co-catalyst gave the by-product 1,2-cyclooctadiol.

Next, cyclohexene oxide was tested. This was because it was believed that cyclooctene oxide is a more stable epoxide, and that the problems observed were caused by the low reactivity of the epoxide. Several examples from literature shows cyclohexene oxide is reduced to the mono-ol faster than cyclooctene oxide.[133,134]

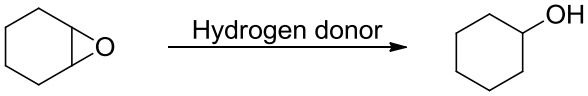



**Figure 6-8: Catalytic transfer hydrogenation of cyclohexene oxide to cyclohexanol was studiet as a test reaction.**

Firstly $NH_4HCO_2$ was tested as a hydrogen donor. Solvent amount was 2 mL to 0.5 mmol substrate and amount of $NH_4HCO_2$ was 3 equivalents. The reaction conditions and results are displayed in Table 6-4.

**Table 6-4: Overview of reaction conditions and results from CTH of cyclohexene oxide with $NH_4HCO_2$.Solvent amount was 2 mL to 0.5 mmol substrate.**

| Solvent | Catalyst | Reaction conditions | Conclusion |
|---|---|---|---|
| [BMIm][$BF_4$] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| | | 80 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| [BMIm][$Tf_2N$] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| | | 80 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| [$C_5O_2$OcIm][$Tf_2N$] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| [BMIm][Cl] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| [$P_{6,6,6,14}$][$Tf_2N$] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| Methanol | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day or 3 days | Good conversion to cyclohexanol, only traces of the epoxide at both conditions. |
| | | 80 °C, 1 day | No starting material left, but material has started to degrade. |
| | Ru/C | 45 °C, 1 day | No reaction |
| Acetic acid | Pd/C | 45 °C, 3 days | No reaction |

Two ILs have been abbreviated in Table 6-4, the structures can be seen in Figure 6-9.

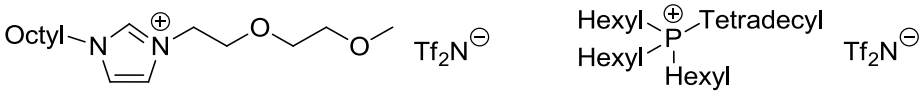



**Figure 6-9: Chemical structure of $[C_5O_2OcIm][Tf_2N]$ (left) and $[P_{6,6,6,14}][Tf_2N]$ (right) used in the CTH.**

None of the ILs tested gave any conversion to cyclohexanol. This might be due to poor solubility of the substrate in the ILs. Using methanol as a solvent was better as this resulted in good conversion, comparable with the conversion described by Varghese *et al*.[124] Too high temperature caused the starting material to degrade.

For the use of HCOOH as hydrogen donor, only the 5:2 preformed complex was tested. The reaction conditions and results are shown in Table 6-5.

**Table 6-5: Overview of reaction conditions and results for the CTH of cyclohexene oxide with the use of HCOOH as hydrogen donor. Solvent amount was 2 mL to 0.5 mmol substrate.**

| Solvent | Catalyst | Reaction conditions | Conclusion |
|---|---|---|---|
| [BMIm][$BF_4$] | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| [BMIm][$Tf_2N$] | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| [$C_5O_2$OcIm][$Tf_2N$] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| [BMIm][Cl] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| [$P_{6,6,6,14}$][$Tf_2N$] | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| | Pd/C | 45 °C, 1 day | Small amount of cyclohexanol was observed, but mostly unconverted material |
| | Ru/C | 45 °C, 1 day | No reaction |
| Methanol | Pd/C | 45 °C, 1 day or 3 days | No reaction |
| Acetic acid | Pd/C | 45 °C, 3 days | No reaction |

For the reaction with HCOOH as the hydrogen donor, only a small conversion was observed when using the phosphonium based IL, though conversion was not as good as the result obtained in methanol using $NH_4HCO_2$ as hydrogen donor. The low reactivity might be due to poor miscibility of the substrate and solvent.

For the use of 2-propanol as hydrogen donor, the reaction conditions and results can be viewed in Table 6-6.

**Table 6-6: Overview of reaction conditions and results obtained by CTH of cyclohexene oxide with the use of 2-propanol as hydrogen donor. Solvent amount was 2 mL to 0.5 mmol substrate.**

| Solvent | Catalyst | Reaction conditions | Conclusion |
|---|---|---|---|
| [BMIm][$BF_4$] | Pd/C, KOH | 45 °C, 1 day | No reaction |
| | Pd/C, HCl (aq) | 45 °C, 1 day | Unknown product was formed |
| [BMIm][$Tf_2N$] | Pd/C, KOH | 45 °C, 1 day | No reaction |
| | Pd/C, HCl (aq) | 45 °C, 1 day | Unknown product was formed |
| Methanol | Pd/C, KOH | 45 °C, 1 day | No reaction |
| | Pd/C, HCl (aq) | 45 °C, 1 day | Unknown product formed |
| - | Pd/C, KOH | 45 °C, 1 day | No reaction |
| | Pd/C, HCl (aq) | 45 °C, 1 day | Unknown product formed |

All reactions with KOH as the co-catalyst gave no reaction. All reactions with HCl(aq) resulted in an unknown product. This might be a mixture of the mono-ol and diol, which was difficult to determine analytically.

Because of the poor results with CTH of cyclooctene oxide and cyclohexene oxide in ILs, methyl cinnamate was tested in a CTH reaction.

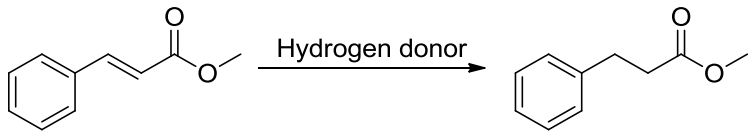



**Figure 6-10: Reduction of methyl cinnamate was tested.**

The following reaction conditions were tested in the reduction of methyl cinnamate:

**Table 6-7: Reaction conditions and results of CTH of methyl cinnamate. Hydrogen donor was $NH_4HCO_2$. Solvent amout was 2 mL to 0.5 mmol solvent.**

| Solvent | Catalyst | Reaction conditions | Conversion |
|---|---|---|---|
| [BMIm][$BF_4$] | $Pd(OAc)_2$ | 45 °C, 1 day | Traces of methyl cinnamate |
| [EMIm][$EtOSO_3$] | $Pd(OAc)_2$ | 45 °C, 1 day | Full conversion |
| [EMIm][$EtOSO_3$] | Pd/C | 45 °C, 1 day | Full conversion |
| Methanol | $Pd(OAc)_2$ | 45 °C, 1 day | No reaction |
| Methanol | Pd/C | 45 °C, 1 day | No reaction |
| [BMIm][$BF_4$] : methanol 1:1 | $Pd(OAc)_2$ | 80 °C, 3 days | Traces of methyl cinnamate |
| [BMIm][$BF_4$] : methanol 1:1 | Pd/C | 80 °C, 3 days | Full conversion |
| [BMIm][$BF_4$] : methanol 1:1 | Ru/C | 80 °C, 3 days | Traces of methyl cinnamate |

As displayed in Table 6-7, CTH of methyl cinnamate was tested under 6 different reaction conditions, 3 gave full conversion, and 3 still contained traces of methyl cinnamate. This proves that the ILs and catalysts chosen can be used in a hydrogenation with $NH_4HCO_2$ as the hydrogen donor. This also indicates that the poor results with reductive opening of the two tested epoxides could be due to poor solubility in the ILs.

## 6.3 Epoxidized glycerol monooleate

Even though the test substrates did not give any good results in a CTH reaction, EGMS and EDAGMS were also tested with the three hydrogen donors and the three different catalysts described previously. The EGMS tested was prepared early in the project, before the final route of epoxidation was found. This EGMS was prepared by epoxidation with *m*-CPBA.[72]

For the use of $NH_4HCO_2$ as a hydrogen donor, the reaction conditions and results can be seen in Table 6-8.

**Table 6-8: Overview of reaction conditions and results for the CTH of EGMS and EDAGMS with the use of $NH_4HCO_2$ as hydrogen donor.**

| Solvent | Catalyst | Reaction conditions | Substrate | Conclusion |
|---|---|---|---|---|
| [BMIm][$Tf_2N$] | $Pd(OAc)_2$ | 80 °C, 1 day | EGMS | No reaction |
| | | | EDAGMS | No reaction |
| | | 80 °C, 1 hour | EGMS | No reaction |
| | | | EDAGMS | No reaction |
| | Ru/C | 80 °C, 1 day | EGMS | No reaction |
| | | | EDAGMS | No reaction |
| | | 80 °C, 1 hour | EGMS | No reaction |
| | | | EDAGMS | No reaction |
| Acetic acid | $Pd(OAc)_2$ | 45 °C, 1 day | EGMS | Small conversion to dihydroxylated product |
| | Pd/C | 45 °C, 1 day | EGMS | Small conversion to dihydroxylated product |
| | Ru/C | 45 °C, 1 day | EGMS | Small conversion to dihydroxylated product |

No reaction was observed in any of the tested reaction conditions when using $NH_4HCO_2$ as a hydrogen donor and [BMIm][$Tf_2N$] as solvent. Using acetic acid as solvent resulted in dihydroxylation. The problems with the formation of dihydroxylated- instead of monohydroxylated product could be due to a catalyst poisoning detected by another in the project. The catalyst poisoning was properbly leftover *m*-chlorobenzoic acid from the epoxidation. This can react with $H_2$ in the presence of for instance Pd in a hydrochlorination reaction yielding benzoic acid.[135,136] This reaction could also be performed in the presence of a hydrogen donor in a catalytic transfer hydrogenolysis.[137] This poisoning should not be present when using the peracetic acid for epoxidation. No reaction of EGMS or EDAGMS in [BMIm][$Tf_2N$] could be due to poor miscibility of the epoxides and the IL, like no reaction was observed for the two epoxide model substrates in the ILs.

For the use of HCOOH as a hydrogen donor, the reaction conditions and results can be seen in Table 6-9. As previously, HCOOH and $Et_3N$ can be added separately (A: ratio 2:5, B: ratio 1:1) or as a preformed complex (C: ratio 5:2).

**Table 6-9: Overview of reaction conditions and results for the CTH of EGMS and EDAGMS with the use of HCOOH as hydrogen donor. HCOOH and $Et_3N$ can be added separately (A: ratio 2:5, B: ratio 1:1) or as a preformed complex (C: ratio 5:2).**

| Solvent | Catalyst | Addition of HCOOH | Reaction conditions | Substrate | Conclusion |
|---|---|---|---|---|---|
| [BMIm][$Tf_2N$] | $Pd(OAc)_2$ | Method A | 30 °C, 1 day | EGMS | No reaction except some hydrolysis |
| | | | | EDAGMS | No reaction |
| | | Method B | 30 °C, 1 day | EGMS | No reaction |
| | | | | EDAGMS | No reaction |
| | | Method C | RT, 1 day | EGMS | No reaction |
| | | | 80 °C, 1 day | EGMS | Unknown product formed |
| | Pd/C | Method C | RT, 1 day | EGMS | Unknown product formed |
| | | | 80 °C, 1 day | EGMS | Unknown product formed |
| | Ru/C | Method C | RT, 1 day | EGMS | Unknown product formed |
| | | | 80 °C, 1 day | EGMS | Unknown product formed |

| Solvent | Catalyst | Addition of HCOOH | Reaction conditions | Substrate | Conclusion |
|---|---|---|---|---|---|
| $[P_{6,6,6,14}][Tf_2N]$ | $Pd(OAc)_2$ | Method C | 60 °C, 1 day | EGMS | No reaction |
| | | | | EDAGMS | No reaction |
| | Pd/C | Method C | 60 °C, 1 day | EGMS | Only reaction observed was some hydrolysis |
| | | | | EDAGMS | No reaction |
| - | $Pd(OAc)_2$ | Method C | 60 °C, 1 day | EGMS | Small conversion to dihydroxylated product |
| | | | | EDAGMS | Small conversion to dihydroxylated product |
| | Pd/C | Method C | 60 °C, 1 day | EGMS | No reaction |
| | | | | EDAGMS | Small conversion to dihydroxylated product |
| Acetic acid | $Pd(OAc)_2$ | Method C | 45 °C, 1 day | EGMS | Small conversion to dihydroxylated product |
| | Pd/C | Method C | 45 °C, 1 day | EGMS | Small conversion to dihydroxylated product |
| | Ru/C | Method C | 45 °C, 1 day | EGMS | Small conversion to dihydroxylated product |

As displayed in Table 6-9 dihydroxylation was a problem under several of the tested reaction conditions. This could be due to the catalyst poisoning by *m*-chlorobenzoic acid previously described. The epoxide was miscible with both $[P_{6,6,6,14}][Tf_2N]$ and acetic acid, whereas immiscible with $[BMIm][Tf_2N]$, which gave no conversion or an unknown product. This again indicated that it was important to have the substrate miscible with the solvent.

For the use of 2-propanol as a hydrogen donor, the reaction conditions and results can be seen in Table 6-10. The amount of 2-propanol was 1.8 equivalents unless otherwise specified. Initally only $[BMIm][Tf_2N]$ was tested as solvent and only Ru/C and HCl(aq) was tested as catalysts

**Table 6-10: Overview of reaction conditions and results for the CTH of EGMS and EDAGMS with the use of 2-propanol as hydrogen donor. Solvent used was $[BMIm][Tf_2N]$**

| Reaction conditions | Substrate | Conclusion |
|---|---|---|
| 80 °C, 1 day | EGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |
| | EDAGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |
| 80 °C, 4 hours | EGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |
| | EDAGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |
| 80 °C, 1 hour | EGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |
| | EDAGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |
| 1.07 equivalents of 2-propanol; 80 °C, 1 hour | EGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |
| | EDAGMS | Hydrolysis and dihydroxylation was observed, no sign of the desired monool |

Hydrolysis and the formation of dihydroxylated product was the only reaction observed when using 2-propanol as the hydrogen donor in [BMIm][$Tf_2N$]. This must be due to the water present in the co-catalyst and the reaction with water was faster than the CTH.

The CTH of EGMS with 2-propanol was also tested in acetic acid as displayed in Table 6-11.

**Table 6-11: Overview of reaction conditions and results of CTH of EGMS with 2-propanol in acetic acid.**

| Catalyst | Reaction conditions | Conclusion |
|---|---|---|
| $Pd(OAc)_2$ | 45 °C, 1 day | DHGMA was observed along with traces of MHGMS |
| Pd/C | 45 °C, 1 day | DHGMS was the only observed product |
| Ru/C | 45 °C, 1 day | DHGMS was the only observed product |

Also performing CTH of EGMS in acetic acid resulted only in the formation of DHGMS when using 2-propanol as the hydrogen donor. This could be due to the water present in the co-catalyst. The use of the homogeneous catalyst $Pd(OAc)_2$ gave faster reaction in the CTH and therefore some MHGMS was observed with this catalyst.

The conclusion of the CTH of EGMS prepared by *m*CPBA is that it was important to have a homogenous reaction system and that the catalyst poisoning has to be removed. To test the system without the catalyst poisoning from *m*chlorobenzpic acid, initial testing with CTH of EGMS prepared with peracetic acid was performed. All these experiments were performed in the acetic acid the epoxide was synthesized in. The results can be seen in Table 6-12. This also eliminated the problem with poor miscibility of the substrate in the solvent.

**Table 6-12: Overview of reaction conditions and results for initial studies of CTH of EGMS prepared with peracetic acid.**

| Hydrogen donor | Catalyst | Reaction conditions | Conclusion |
|---|---|---|---|
| $NH_4HCO_2$ | $Pd(OAc)_2$ | 45 °C, 1 day | A small increase in the amount of DHGMS was observed and traces of MHGMS, but mainly no reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | No reaction |
| HCOOH:$Et_3N$ 5:2 complex | $Pd(OAc)_2$ | 45 °C, 1 day | A small increase in the amount of DHGMS and traces of MHGMS was observed but mainly no reaction |
| | Pd/C | 45 °C, 1 day | Small traces of MHGMS but mainly no reaction was observed |
| | Ru/C | 45 °C, 1 day | No reaction |
| 2-propanol | $Pd(OAc)_2$ | 45 °C, 1 day | A small increase in the amount of DHGMS was observed but mainly no reaction |
| | Pd/C | 45 °C, 1 day | No reaction |
| | Ru/C | 45 °C, 1 day | A small increase in the amount of DHGMS was observed |

As displayed in Table 6-12 still no positive results came out of the CTH of EGMS. The results with the homogeneous catalyst $Pd(OAc)_2$ gave a small conversion of EGMS, though mainly to the dihydroxylated product. This could also be the acetoxy-hydroxy compound as a result of an attack from acetic acid. Formic acid and Pd/C resulted in some conversion to the desired MHGMS, but the overall conclusion was that with the tested reaction conditions, it was not possible to obtain a reductive opening of the epoxide. This could be due to left-over peracetic acid in the reaction mixture was easier reduced than EGMS.

# Chapter 7
# Hydrogenation using molecular hydrogen

As mentioned in Chapter 6, hydrogenation experiments were also tested using molecular hydrogen. Unless specified, all hydrogenation experiments with molecular hydrogen were performed on EGMS synthesized in the way described in Chapter 5.

## 7.1 Using Pd/C as catalyst

When Pd/C was applied as catalyst, gas formation was observed from the reaction mixture. It was tested if it was the palladium or the active carbon that was responsible for this, by addition of active carbon to a reaction mixture. This did not give any gas formation, so it was the palladium that was responsible for the gas formation. When Pd/C was used as a catalyst, a small amount was added, and after the gas formation stopped, the rest of the catalyst was added.

The first test of hydrogenation was performed with small amount of Pd/C (5 g to 1500 g reaction mixture) and low pressure (5 bar). The temperature in the reaction mixture increased in the beginning. This was a sign of hydrogen being consumed fast. Later in the reaction the temperature decreased to RT again as a sign of slower consumption of hydrogen. Already after 10 minutes it was clear that the major product was not MHGMS as desired, but glycerol monostearate (GMS). The formation of GMS can either be formed directly from the epoxide or go through a MHGMS intermediate (see Figure 7-1). It was important to note that some GMS was also present in the starting material (GMO) and that 10 % acetylated GMS is present in SNS. But as GMS has no plasticizing effect, it is important not to further increase the amount of GMS. After 10 minutes, the conversion to GMS was 60 % and only 20 % MHGMS. Only 2 % of EGMS was left in the reaction mixture. The amount of DHGMS and

free fatty acids were about the same as for the starting material. Samples taken after 1.5 hours and 2.5 hours showed no further reaction had occurred.

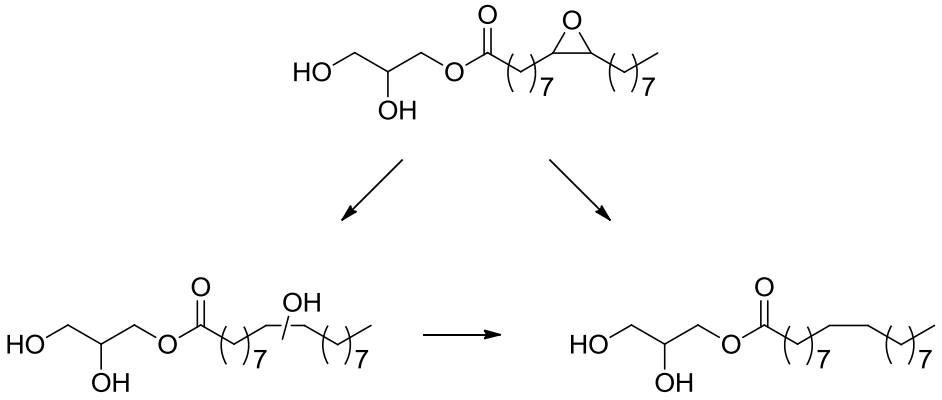



**Figure 7-1: EGMS can be reduced to either the desired MHGMS (left) or to GMS (right).**

In the next experiment only 2 bar $H_2$(g) was applied. After 45 minutes the amount of GMS was higher than the amount of EGMS present in the reaction mixture. After 1.5 hours 52 % of the EMGS was converted to GMS and 25 % to MHGMS. 12% EGMS was unreacted. After 2 hours a little EGMS was still present showing that the conversion was slower at reduced pressure. The amount of DHGMS did not change during the reaction.

Lowering the catalyst amount to 1/10 of the amount used previously and adding first 2 bar $H_2$(g) then 5 bar $H_2$ (g) did not help, as no conversion was observed at all. This was probably due to deactivation of the catalyst by the strong oxidant peracetic acid. Adding 4 times this amount of catalyst and 2 bar $H_2$(g) gave only little conversion, mostly to GMS but also small amounts of MHGMS were observed. After 2 hours the amount of unconverted starting material was 42 % and the amount of GMS and MHGMS was 31 % and 13 % respectively. Running this experiment in a smaller autoclave resulted in no conversion at all. A small increase in the amount of catalyst and pressure gave the same result, though a slight conversion was observed in the small autoclave while no reaction was observed in the bigger autoclave. The conversion observed was even smaller than the one observed previously. Too

small amounts of Pd/C and too low pressure were therefore concluded not to be efficient for the hydrogenation of EGMS.

In the next experiments, the Pd/C amount was kept constant at 4 g to 1500 g reaction mixture. The pressure of $H_2$(g) was tested at both 10 and 15 bar. At 10 bar there was only a small amount of EGMS was left (7 %) after 2 hours, but the main product was again GMS (45 %), though the amount of MHGMS was higher than previous experiments (36 %). For 15 bar the result was almost the same. There was not much difference between the two experiments.

High amount of catalyst was also tested. 0.5 g Pd/C to 20 g reaction mixture and 5 bar resulted in good conversion already after 1 hour with only 4 % unreacted starting material left. Unfortunately the primary product was still GMS (54 %), but the conversion to MHGMS was also high (35 %).

On overview of the reductions of EGMS with Pd/C and $H_2$(g) can be seen in Table 7-1. The conclusion was that high amount of catalyst was needed to have good conversion. GMS was the main product in all reduction experiments with Pd/C and $H_2$(g).

**Table 7-1: Overview of the reduction of EGMS with $H_2$(g) and Pd/C.**

| Reaction conditions | Conclusion |
|---|---|
| 5 g Pd/C to 1500 g reaction mixture, 5 bar $H_2$(g) | 60 % GMS and 20 % MHGMS was observed. |
| 5 g Pd/C to 1500 g reaction mixture, 2 bar $H_2$(g) | 52 % GMS and 25 % MHGMS was observed. |
| 0.5 g Pd/C to 1500 g reaction mixture, 2-5 bar $H_2$(g) | No reaction observed. |
| 2 g Pd/C to 1500 g reaction mixture, 2 bar $H_2$(g) | 31 % GMS and 13 % MHGMS was observed. |
| 4 g Pd/C to 1500 g reaction mixture, 3 bar $H_2$(g) | Almost the same as the previous experiment. |
| 4 g Pd/C to 1500 g reaction mixture, 10 or 15 bar $H_2$(g) | 45 % GMS and 36 % MHGMS |
| 0.5 g Pd/C to 20 g reaction mixture, 5 bar $H_2$(g) | 54 % GMS and 35 % MHGMS. |

## 7.2 Removal of peracetic acid

It was tested if removal of the peracetic acid before hydrogenation could improve the reaction, although it was suggested in 1952 that peracetic acid should not have a negative effect on the reductive opening of an epoxide.[138] This was firstly tested by addition of $MnO_2$ to reduce peracetic acid to acetic acid, see Figure 7-2.

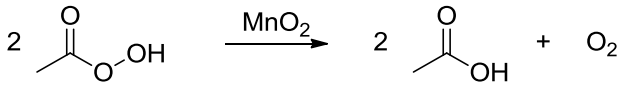



**Figure 7-2: $MnO_2$ catalyzes the formation of $O_2$ from peracetic acid**

The addition if $MnO_2$ causes a heavily gas formation as expected. After the gas formation had stopped, the reaction mixture was filtered before hydrogenating using 4 g Pd/C and 10 bar $H_2$(g). This however was not a good idea, as almost no conversion of EGMS was observed. This must be due to the catalyst deactivation by manganese salts, due to binding of the palladium to manganese.

Lowering the amount of peracetic acid was also performed by adding less in the epoxidation reaction, even though this resulted in longer reaction time as described in the previous chapter. 5 g Pd/C and 5 bar $H_2$(g) was tested. The main product from this was GMS, but a little less was formed compared to previous experiments. After 2 hours the result was 41 % GMS, 36 % MHGMS and unconverted EGMS accounted for 13 %. Also 2 g Pd/C and 5 bar was tested. The main product was again GMS, but almost no reaction of EGMS was observed. Only very small conversion to MHGMS was observed. Adding even less peracetic acid during the epoxidation reaction resulted in only small conversion after 2 hours. A sample taken the next day indicated that the formation of GMS and DHGMS was a problem, but still good conversion to MHGMS was observed. 38 % of the material was converted to MHGMS and 35 % to GMS. The amount of DHGMS had increased to 16 % and unreacted starting material was 10 %. Adding too little peracetic acid to react with all GMO and reacting overnight still gave problems with no conversions, but the

long reaction time for epoxidation had resulted in high formation of DHGMS. The amount of DHGMS was however not increased by the hydrogenation.

Removal of peracetic acid was tested by addition of acetaldehyde before the hydrogenation. Addition of acetaldehyde to peracetic acid results in the formation of acetic acid,[139] see Figure 7-3. Hydrogenation conditions was 2 g Pd/C and 5 bar $H_2$(g). This resulted in GMS being the main product after 2 hours with 41 %. The amount of MHGMS was 18 % and unreacted EGMS accounted for 27 %.

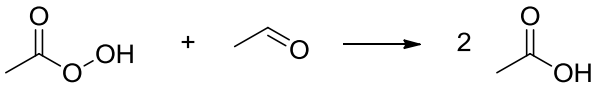



**Figure 7-3: Peracetic acid is reduced to acetic acid by the reaction of acetaldehyde.**

It was also tested to remove the acetic acid from the reaction mixture by extraction of the EGMS from the reaction mixture with heptane and washing with $NaHCO_3$. Only little conversion to MHGMS was observed, but the amount of GMS was not increased. Hydrogenation of EGMS in acetic acid prepared by another method had previously given good results from another in the project, so it was not likely that acetic acid was the main problem for the hydrogenation.

Ultrasound treatment of the reaction mixture prior to reduction was also tested. Using a Pd/C catalyst, the primary conversion was to GMS. A small amount of MHGMS was also observed, but it was concluded that ultrasound treatment did not help. Also treatment with active carbon before reduction with Pd/C did not help.[140]

An overview of the reduction experiments can be seen in Table 7-2.

**Table 7-2: Overview of the reduction of EGMS after removal of peracetic acid.**

| Reaction conditions | Conclusion |
|---|---|
| Addition of $MnO_2$ | Almost no conversion. |
| Lower amount of peracetic acid in the epoxidation reaction | 41 % GMS and 36 % MHGMS was observed in one experiment and 35 % GMS and 38 % MHGMS in another experiment. |
| Addition of acetaldehyde | 41 % GMS and 18 % MHGMS was observed |
| Extraction of EGMS from reaction mixture | Only small conversion was observed. |
| Ultrasound treatment | Only small conversion was observed. |

## 7.3 Using other catalysts and substrates

Other catalysts have also been tested. Using a Nickel catalyst (Pricat9910 from Johnson Matthey) and 20 bar $H_2$(g) only resulted in hydrolysis, there was no sign of MHGMS at all. Raney Nickel was also tested at 20 bar. No reaction was observed after 2 hours, so the temperature was increased to 40 °C. After 2 hours at this temperature, mainly conversion to DHGMS was observed, only small amounts of MHGMS and a small increase in the amount of GMS was observed. It is noteworthy that addition of a Nickel catalyst does not give gas formation when added, and all catalyst can therefore be added at once.

Applying Pt/C as catalyst resulted in a small increase in the amount of DHGMS but otherwise no reaction was observed. Pd/$BaSO_4$ was also tested, but this resulted in primary GMS and only little conversion to MHGMS. The reaction time was also longer compared to when Pd/C was used, after 2 hours almost no conversion was observed. Adding $BaSO_4$ before the hydrogenation to further decrease the activity of the catalyst and then using Pd/C as the catalyst resulted in primarily GMS, but some MHGMS could also be observed after 20 hours of reaction. Rh/C gave no conversion after 2 hours, but after 20 hours, a very small amount of MHGMS was observed. Also a small increase in the amount of DHGMS was observed, but the amount of GMS was not increased.

Also Ru/C was tested, but after 2 hours no conversion was observed and after 20 hours the only conversion observed was an increase in the amount of DHGMS.

A summary of the experiments with other catalysts is shown in Table 7-3.

**Table 7-3: Overview of the reduction of EGMS with other catalysts.**

| Reaction conditions | Conclusion |
|---|---|
| Nickel catalyst (Pricat 9910) | No sign of MHGMS |
| Raney Nickel | Mainly conversion to DHGMS |
| Pt/C | Small increase in DHGMS was observed. |
| $Pd/BaSO_4$ | Primarily GMS was observed. |
| $BaSO_4$ before hydrogenation with Pd/C as catalyst | Primarily GMS was observed. |
| Rh/C | Only a very small conversion was observed. |
| Ru/C | Small increase in DHGMS was observed. |

Because of the poor results with the hydrogenation of EMGS to MHGMS, the reaction was tested using EDAGMS as substrate. This was prepared with peracetic acid so only the substrate was different from previous experiments. Also here the reduction to the saturated compound could be observed (15 %), but the conversion to the mono-hydroxy compound was 32 %. The amount of epoxide left after 2 hours was 43 %. The next day, the amount of monoglyceride of the saturated fatty acid had increased to 22 %, but the amount of mono-hydroxy compound was still high (50 %). The amount of unconverted starting material was 12 %.

Furthermore, testing of hydrogenation of epoxidized oleic acid was tested. This did not result in the desired mono-hydroxy compound as described in literature.[138] No conversion was observed of the starting material.

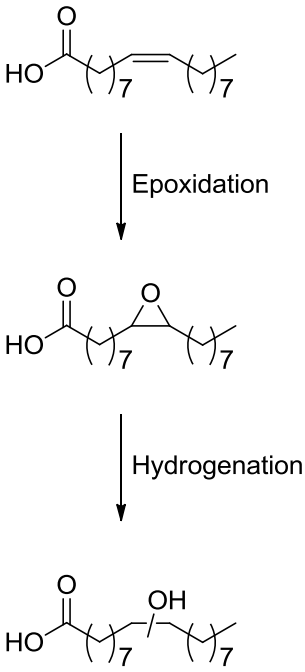



**Figure 7-4: Epoxidation followed by a hydrogenation of oleic acid. Adapted from Mach and Bickford.**[138]

# Chapter 8
# Conclusion and outlook

The increasing concern for the use of phthalates have led to the discovery of several alternatives, one of them being Grindsted® SOFT-N-SAFE (SNS) (to the left in Figure 8-1) developed by Danisco A/S (now known as DuPont Nutrition Biosciences Aps). An analogue (SNS-A) (to the right in Figure 8-1) was developed and the objective of this PhD study was, in collaboration with the company and another university, to develop a cheap and sustainable synthetic pathway for SNS-A. A three step pathway consisting of epoxidation, hydrogenation and acetylation of the starting material glycerol monooleate (GMO) was suggested early in the project.


**Figure 8-1: Chemical structures of SNS (left) and SNS-A (right).**

The new reaction pathway is shown in Figure 8-2.

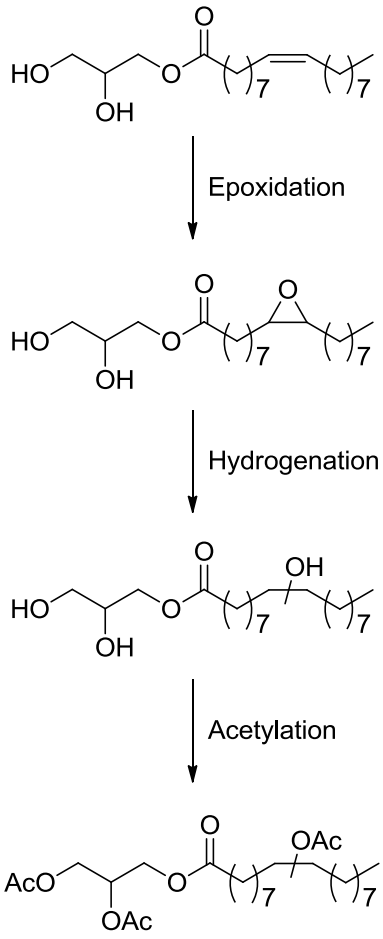



**Figure 8-2: Schematic overview of the final suggested synthetic route for SNS-A.**

A patent for this process has been filed during the project.[141]

There were three goals for this PhD study: finding an ionic liquid (IL) suitable for phase separation of the product and suitable as a reaction media for one or more of the reactions and develop and optimize an epoxidation and hydrogenation method.

Several ILs were synthesized or purchased and tested for the phase separation properties of SNS and the intermediates from the synthesis of SNS. It was desired to have an IL where the starting material was miscible, as this would

give homogenous reaction conditions. Furthermore, it was also important that the IL was non-miscible with water, to protect the glycerol ester bond from hydrolysis. It was not possible to find an IL from which SNS could be separated. Only one IL showed phase separation properties where a homogeneous epoxidation and hydrogenation reaction could have been performed. This was trihexyltetradecyl phosphonium bis(trifluoromethylsulfonyl)amide ($[P_{6,6,6,14}][Tf_2N]$). If simple phase separation of any of the products were to be performed in any of the other tested ILs, this would result in heterogeneous reaction conditions. This could give longer reaction time and the risk of hydrolysis would be increased.

The epoxidation method was tested using two different methods; catalytic epoxidation and epoxidation using peracetic acid. The catalytic epoxidation was tested with the functionalized heteropoly acid catalyst $[BMIm]_3PW_{12}O_{40}$, hydrogen peroxide as the oxidant and different ILs, where phase separation was possible, as the solvent. An IL was chosen to optimize the epoxidation reaction, but unfortunately it was not possible to obtain a satisfying result using the epoxidation method. It was therefore concluded that this method would not be suitable for possible industrial implementation and it was therefore nor pursued further. Applying peracetic acid as the oxidant and acetic acid as the solvent showed, on the other hand, very promising results already in the initial experiments. Optimizing the reaction conditions gave some satisfying results, as the amount of peracetic acid used was low, the conversion was high, the temperature was low, the reaction time short, the amount of unwanted side-reactions was low and the reproducibility was high. Testing of the system in a 2 L reaction mixture scale showed the same satisfying result every time. It could thus be concluded that epoxidation using peracetic acid in acetic acid was a really good method. It is important to note that epoxidation in acetic acid with peracetic acid, which contained some water, did not give problems with hydrolysis of the glycerol backbone with the short reaction times applied.

The heat of reaction from the epoxidation reaction has to be measured before a safe up-scaling of the process can be performed.

The hydrogenation of the epoxide to a mono-hydroxy compound was tested using either a hydrogen donor, catalytic transfer hydrogenation (CTH) or molecular hydrogen gas. For CTH three different catalysts (Pd/C, Ru/C and $Pd(OAc)_2$), three different hydrogen donor ($NH_4HCO_3$, 2-propanol and formic acid) and several solvents, many of them ILs, were tested for different substrates or the epoxide from the project. No good results were obtained from this method, and it was concluded that CTH was unsuited for reductive opening of 9,10-epoxy glycerol monostearate (EGMS) in the project. Using molecular hydrogen gas also gave problems, as the main product obtained was the saturated monoglyceride instead of the mono-hydroxy substituted monoglyceride. Several different catalysts and reaction conditions were tested, but either with formation of the saturated monoglyceride or with no reaction observed at all.

Further investigations on the hydrogenation must be performed to find a suitable method for the reductive ring-opening of the epoxide. It is important that the hydrogenation can be performed in acetic acid, as this is the solvent for both the first and the third step of the process. Furthermore it is important to avoid the formation of the saturated monoglyceride.

The overall conclusion for this project is that an industrially viable epoxidation protocol has been developed.

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# Experimental section

All reagents were commercially available or supplied by Danisco A/S and were used as supplied unless specified.

Samples for GC was silylated prior to analysis by GC. The silylation was performed according to analysis regulatory from Danisco A/S.[142] 50 mg sample was dissolved in 12 mL heptane:pyridine (volume ration 2:1). From this, 500 µL was mixed with 100 µL of a mixture of *N*-Methyl-*N*-trimethylsilyl-trifluoroacetamide (MSTFA) and Trimethylchlorosilane (TMCS) (volume ratio 99:1). This was heated to 60 °C for 15 minutes before analysis on GC. All analysis was compared to GC chromatograms of the known products (reference samples).

Two different GCs have been used in this project when performing analysis at DTU or Danisco A/S, respectively.

GC at DTU: Agilent Technologies 7890A GC equipped with FID, cool-on-column injector and a high-temperature DB-5HT capillary column (J&WScientific, 15 m × 0.32 mm × 0.25 µm ((5 mol% phenyl)-methylpolysiloxane) joined with a precolumn (or guard-column, J&W Scientific, 1 m × 0.53 mm, of fused deactivated silica). Program: heat to 50 °C and hold for 1 minute, heat to 180 °C at 15 °C/minute, heat to 300 °C at 5 °C/minutes, heat to 350 °C at 30 °C/minute and hold the temperature for 4 minutes.

GC at DuPont Nutrition Biosciences Aps: Varian 3900 GC equipped with FID and Varian CP-Sil 5 CB lowbleed column, 15m x 0.15 mm id ((5 mol% phenyl)-methylpolysiloxane): Program 50 °C and hold for 1.5 minutes, heat to 200°C at 20 °C/minute, heat to 240 °C at 10 °C/minute, heat to 350 °C at 12 °C/minute and hold for 6 minutes.

For the recording of $^{1}$H NMR and $^{13}$C NMR either a Varian Mercury-300 spectrometer (operating at 300 MHz for proton and 75 MHz for carbon) or a

Bruker Avance III spectrometer (operating at 600MHz for proton, 150 MHz for carbon and 243 MHz for phosphor were used. Chemical shifts (δ) are given in ppm relative to TMS ($^{1}$H NMR) or with deutorated solvents ($^{13}$C NMR) as internal standard.

Elemental analyses were performed with a CE Instrument: FLASH 1112 series EA, at the Microanalytical Laboratory, Department of Chemistry, University of Copenhagen.

## Synthesis of 1-butyl-3-methyl imidazolium bis(trifluoromethylsulfonyl)amide [BMIm][$Tf_2N$]

1-butyl-3-methyl imidazolium chloride (95 % pure, 6.35 g, 34.5 mmol) was dissolved in demineralized $H_2O$ (25 mL) and $LiNTf_2$ (99 % pure, 10.31 g, 35.6 mmol) demineralized $H_2O$ (25 mL) was added. This instantly resulted in two phases. The reaction mixture was stirred for a day before the aqueous phase was decanted off and the crude mixture was washed with water until no $Cl^-$ could be detected (tested with $AgNO_3$).

Yield: > 99 %

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 8.45 (d, J = 6.3 Hz, 1H), 7.22 (ddt, J = 5.6, 3.7, 1.7 Hz, 2H), 4.01 (t, J = 7.4 Hz, 2H), 3.76 (s, 3H), 1.69 (dq, J = 12.6, 7.6 Hz, 2H), 1.20 (dq, J = 14.7, 7.3 Hz, 2H), 0.92 – 0.63 (m, 3H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ 135.73, 123.79, 122.53, 49.79, 36.07, 31.86, 19.21, 19.02.

## Synthesis of 1-butyl-3-methyl imidazolium tetrafluoroborate [BMIm][$BF_4$]

1-butyl-3-methyl imidazolium chloride (95 % pure, 11.71 g, 63.7 mmol) was dissolved in demineralized $H_2O$ (30 mL) and an aqueous solution of $HBF_4$ (48 % pure, 10 mL, 76.7 mmol) was added dropwise. The reaction mixture was allowed to stir at room temperature for a day before extraction with

dichloromethane (2 × 60 mL). The organic phase was then washed with water until the washing water was neutral.

Yield: > 99 %

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 8.80 (s, 1H), 7.38. (s, 1H), 7.32 (s, 1H), 4.15 – 4.20 (m, 2H), 3.90 (s, 1H), 1.80 –1.90 (m, 2H), 1.30 – 1.40 (m, 2H), 0.90 – 1.00 (m, 3H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ136.66, 123.85, 122.32, 50.06, 45.91, 36.49, 32.10, 19.88, 13.51

## Synthesis of methanesulfonic acid 2-(2-methoxyethoxy)-ethyl ester

2-(2-methoxyethoxy)ethanol (99 % pure, 17.9 mL 150.9 mmol) and triethylamine (99 % pure, 21.4 mL, 151.9 mmol) was mixed in freshly distilled diethylether (250 mL) under an inert atmosphere. The mixture was then cooled to 0 °C before mesyl chloride (98 % pure, 12.0 mL, 151.9 mmol) was added dropwise. A white precipitate was formed, which after 20 hours was removed by filtration. The solvent was removed *in vacuo* from the resulting yellow liquid. The crude product was dissolved in dichloromethane (110 mL) and washed with water (3 × 50 mL) before isolation by removing the dichloromethane *in vacuo*.

Yield: > 99 %

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 5.31 (s, 1H), 4.45 – 4.36 (m, 2H), 3.80 – 3.75 (m, 2H), 3.69 – 3.65 (m, 2H), 3.57 – 3.53 (m, 2H), 3.38 (s, 3H), 3.07 (s, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 71.82, 70.60, 69.21, 69.05, 59.01, 37.66.

## Synthesis of methanesulfonic acid 2-(2-(2-methoxyethoxy)-ethoxy)ethyl ester

2-(2-(2-methoxyethoxy)ethoxy)ethanol (99 % pure, 410.2 g mL 2.47 mol) and triethylamine (99 % pure, 255.5 g, 2.50 mol) were mixed in freshly distilled diethylether (4.5 L) under an inert atmosphere. The mixture was cooled to 0 °C before mesyl chloride (98 % pure, 289.7 g, 2.48 mol) was added dropwise. A white precipitate was formed, which after 72 hours was removed by filtration. The solvent was removed *in vacuo* from the resulting yellow liquid. The crude product was dissolved in dichloromethane (750 mL) and washed with water (3 × 250 mL) before isolation by removing the dichloromethane *in vacuo*.

Yield: > 99 %

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 4.40 – 4.36 (m, 2H), 3.78 – 3.75 (m, 2H), 3.70 – 3.67 (m, 2H), 3.67 – 3.61 (m, 4H), 3.55 – 3.52 (m, 2H), 3.38 (s, 3H), 3.07 (d, J = 3.1 Hz, 3H).

## Synthesis of 1-octylimidazole

Imidazole (99.5 % pure, 75.52 g, 1.03 mol), toluene (1 L), tetraethylammonium iodide (98 % pure, 52.53 g, 0.2 mol) and NaOH (99 % pure, 137.02 g, 3.39 mol) were mixed and heated to 115 °C. Octyl bromide (99 % pure, 218.85 g, 1.12 mol) was slowly added and the reaction mixture was stirred at reflux (115 °C) for 16 hours. After cooling to RT, demineralized $H_2O$ (1 L) was added and the phases were separated. The aqueous phase was extracted with ethyl acetate and the combined organic phases were washed with brine (200 mL) and dried over $Na_2SO_4$. The solvent was removed *in vacuo*.

Yield: 179.06 g (90 %)

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 7.45 (s, 1H), 7.28 – 7.07 (m, 1H), 6.90 (s, 1H), 3.91 (t, J = 7.2 Hz, 2H), 1.84 – 1.69 (m, 2H), 1.42 – 1.16 (m, 12H), 0.88 (dd, J = 8.9, 5.1 Hz, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 137.06, 129.35, 129.05, 47.06, 31.73, 31.09, 29.10, 29.04, 26.57, 22.61, 14.06.

## Synthesis of 1,3-bis-octyl imidazolium bis(trifluoromethyl-sulfonyl)amide

1-octylimidazole (64.99 g, 360.5 mmol), toluene (350 mL), tetraethylammonium iodide (98 % pure, 18.12 g, 69.1 mmol) and NaOH (99 % pure, 42.80 g, 1.06 mol) were mixed and heated to 110 °C. Octyl bromide (99 % pure, 80.12 g, 410.7 mol) was slowly added and the reaction mixture was stirred at reflux (110 °C) for 16 hours. After cooling to RT, demineralized $H_2O$ (80 mL) was added and the phases were separated. The aqueous phase was extracted with ethyl acetate (3 × 100 mL) and the combined organic phases were washed with brine (200 mL). The solvent was removed *in vacuo*. The crude product was dissolved in dichloromethane (400 mL) before $LiNTf_2$ (99 % pure, 108.7 g, 374.9 mmol), dissolved in demineralized $H_2O$ (400 mL), was slowly added. The reaction mixture was stirred for 2 hours at RT before separating the two phases and removing the solvent *in vacuo*.

Yield: 150.72 g (73 %)

$^1$H NMR (600 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.02 (s, 1H), 6.91 (s, 1H), 3.99 – 3.86 (m, 2H), 3.69 – 3.60 (m, 2H), 3.38 (dd, J = 12.9, 6.2 Hz, 2H), 2.95 (dd, J = 19.8, 12.1 Hz, 2H), 1.81 – 1.42 (m, 20H), 0.91 – 0.80 (m, 6H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 129.04, 128.23, 125.31, 48.35, 47.34, 33.19, 32.82, 31.88, 31.72, 29.29, 29.01, 27.77, 26.96, 26.52, 25.76, 22.65, 22.60, 14.08, 14.04.

## Synthesis of 1-methyl-3-octylimidazolium bis(trifluoro-methylsulfonyl)amide

1-methylimidazole (99.5 % pure, 16 mL, 199.7 mmol), toluene (200 mL), tetraethylammonium iodide (98 % pure, 10.96 g, 41.8 mmol), NaOH (99 % pure, 25.17 g, 623.0 mmol) and octyl bromide (99 % pure, 46.41 g, 237.9 mol) were mixed under an inert atmosphere and heated to reflux for 16 hours. After cooling to RT, $H_2O$ (150 mL) was added and the phases were separated. The aqueous phase was extracted with ethyl acetate (3 × 50 mL) and the combined organic phases were washed with $H_2O$ (50 mL). The solvent was removed *in vacuo*. The crude product was dissolved in dichloromethane (250 mL) before

$LiNTf_2$ (99 % pure, 66.30 g, 228.7 mmol), dissolved in demineralized $H_2O$ (250 mL), was slowly added. The reaction mixture was stirred for 3 hours at RT before separating the two phases and removing the solvent *in vacuo*.

Yield: > 99 %

$^1H$ NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.07 (m, 3H), 2.35 (m, 5H), 1.37 – 1.14 (m, 12H), 0.88 (d, J = 3.7 Hz, 3H).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ 137.89, 129.05, 128.24, 125.32, 53.43, 31.84, 29.49, 29.34, 29.18, 22.68, 21.46, 14.10.

## Synthesis of 2-methyl-1,3-bis-octyl imidazolium bis(trifluoromethylsulfonyl)amide

2-methylimidazole (98 % pure, 14.19 g, 199.7 mmol), toluene (200 mL), tetraethylammonium iodide (98 % pure, 9.08 g, 41.75 mmol), NaOH (99 % pure, 22.10 g, 623.0 mmol) were mixed and octyl bromide (99 % pure, 70.01 g, 237.9 mol) was slowly added and the reaction mixture was heated to reflux for 16 hours. After cooling to RT, $H_2O$ (150 mL) was added and the phases were separated. The aqueous phase was extracted with ethyl acetate (3 × 50 mL) and the combined organic phases were washed with demineralized $H_2O$ (150 mL). The solvent was removed *in vacuo*. The crude product was dissolved in dichloromethane (200 mL) before $LiNTf_2$ (99 % pure, 50.52 g, 228.7 mmol), dissolved in demineralized $H_2O$ (200 mL), was slowly added. The reaction mixture was stirred for 3 hours at RT before separating the two phases and removing the solvent *in vacuo*.

Yield: > 99 %

$^1H$ NMR (600 MHz, $CDCl_3$): δ 7.25 (t, J = 7.6 Hz, 1H), 7.16 (dd, J = 14.4, 7.3 Hz, 1H), 3.86 – 3.73 (m, 4H), 2.36 (d, J = 6.3 Hz, 3H), 1.72 (dd, J = 14.1, 7.1 Hz, 2H), 1.36 – 1.12 (m, 22H), 0.88 (t, J = 6.9 Hz, 6H).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ 137.88, 129.05, 128.24, 125.31, 53.42, 46.25, 31.74, 30.68, 29.12, 26.60, 22.61, 21.46, 14.06, 12.78.

## Synthesis of 1-(2-(2-methoxyethoxy)ethyl) imidazole

Tetraethylammonium bromide (98 % pure, 6.3 g, 29.4 mmol) was dispensed in demineralized $H_2O$ (50 mL) and cooled to 0 °C before NaOH (97 % pure, 37.28 g, 904.1 mmol) was added. When most of the NaOH was dissolved, imidazole was added (99.5 % pure, 8.09 g, 118.3 mmol), followed by methanesulfonic acid 2-(2-methoxyethoxy)ethyl ester (23.85 g, 120.3 mmol). The mixture was stirred for 15 hours before adding demineralized $H_2O$ (50 mL) and extracting with dichloromethane (100 mL + 4 × 50 mL). The product was isolated by removing the solvent *in vacuo*.

Yield: 17.43 g (87 %)

$^1$H NMR (600 MHz, $CD_3CN$): δ 7.48 (s, 1H), 7.03 (d, J = 24.8 Hz, 1H), 6.90 (s, 1H), 4.09 (t, J = 5.2 Hz, 2H), 3.69 (t, J = 5.2 Hz, 2H), 3.54 (dd, J = 10.4, 6.4 Hz, 2H), 3.47 – 3.41 (m, 2H), 3.28 (d, J = 8.0 Hz, 3H).

$^{13}$C NMR (151 MHz, $CD_3CN$): δ 138.61, 129.41, 120.60, 118.38, 72.57, 71.08, 58.99, 47.59.

## Synthesis of 1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl) imidazole

Tetraethylammonium bromide (98 % pure, 3.02 g, 14.07 mmol) was dispensed in demineralized $H_2O$ (180 mL) and cooled to 0 °C before NaOH (97 % pure, 145.9 g, 3.54 mol) was added. When most of the NaOH was dissolved, imidazole was added (99.5 % pure, 32.23 g, 471.1 mmol), followed by methanesulfonic acid 2-(2-(2-methoxyethoxy)ehoxy)ethyl ester (113.49 g, 468.4 mmol). The mixture was stirred for 15 hours before extracting with dichloromethane (4 × 100 mL). The product was isolated by removing the solvent *in vacuo*.

Yield: 98.89 g (96 %)

$^1$H NMR (600 MHz, $CDCl_3$): δ 7.55 – 7.52 (m, 1H), 7.04 (dt, J = 1.8, 1.0 Hz, 1H), 7.00 (dt, J = 2.4, 1.2 Hz, 1H), 4.11 (t, J = 5.2 Hz, 2H), 3.77 – 3.70 (m, 2H), 3.64 – 3.57 (m, 6H), 3.57 – 3.50 (m, 2H), 3.40 – 3.36 (m, 3H).

## Synthesis of 1,3-bis-(2-(2-methoxyethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)amide

1-(2-(2-methoxyethoxy)ethyl) imidazole (85.0 g, 499.4 mmol) and methanesulfonic acid 2-(2-methoxyethoxy)ethyl ester (99.7 g, 502.9 mmol) were mixed under an inert atmosphere and heated to 60 °C for 5 days. The reaction mixture was cooled to RT before being dissolved in dichloromethane (500 mL). $LiNTf_2$ (99 % pure, 148.1 g, 510.7 mmol), dissolved in demineralized $H_2O$ (500 mL), was slowly added. The reaction mixture was stirred for 4 hours at RT before separating the two phases. The aqueous phase was extracted with dichloromethane (3 × 40 mL) before the solvent from the combined organic phases were removed *in vacuo*.

Yield: 220.85 g (80 %)

$^1$H NMR (600 MHz, $CDCl_3$): δ 8.82 (s, 1H), 7.41 (s, 1H), 7.15 (s, 1H), 4.36 – 4.44 (m, 4H), 3.82 – 3.90 (m, 4H), 3.61 – 3.69 (m, 4H), 3.49 – 3.57 (m, 4H), 3.36 – 3.44 (m, 6H).

## Synthesis of 1,3-bis-(2-(2-(2-methoxyethoxy)ethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)amide

1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl) imidazole (66.14 g, 308.7 mmol) and methanesulfonic acid 2-(2-(2-methoxyethoxy)ethoxy)ethyl ester (76.46 g, 315.6 mmol) were mixed under an inert atmosphere and heated to 60 °C for 3 days. The reaction mixture was then cooled to RT before being dissolved in dichloromethane (350 mL). $LiNTf_2$ (99 % pure, 105.0 g, 369.5 mmol), dissolved in demineralized $H_2O$ (350 mL), was slowly added. The reaction mixture was stirred for 16 hours at RT before separating the two phases. The aqueous phase was extracted with dichloromethane (2 × 100 mL) before the solvent from the combined organic phases was removed *in vacuo*.

Yield: 174.52 g (89 %)

$^1$H NMR (600 MHz, $CDCl_3$): δ 8.83 (s, 1H), 7.50 (t, J = 4.8 Hz, 2H), 4.41 – 4.32 (m, 4H), 3.85 (dd, J = 11.5, 6.8 Hz, 4H), 3.69 – 3.57 (m, 12H), 3.55 (ddd, J = 9.0, 4.3, 2.5 Hz, 4H), 3.40 – 3.31 (m, 6H).

## Synthesis of 1-methyl-3-(2-(2-methoxyethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)amide

1-methylimidazole (99 % pure, 70 mL, 435.2 mmol) and methanesulfonic acid 2-(2-methoxyethoxy)ethyl ester (85.1 g, 429.3 mmol) were mixed under an inert atmosphere and heated to 60 °C for 1 day before cooled to RT. The reaction mixture was dissolved in dichloromethane (400 mL) before $LiNTf_2$ (99 % pure, 128.3 g, 442.5 mmol), dissolved in demineralized $H_2O$ (400 mL), was slowly added. The reaction mixture was stirred for 72 hours before extracting with dichloromethane. The solvent was removed *in vacuo*.

Yield: > 99 %

$^1$H NMR (600 MHz, $CDCl_3$): δ 8.78 (s, 1H), 7.56 (s, 1H), 7.46 (t, J = 1.7 Hz, 1H), 4.40 – 4.30 (m, 2H), 3.83 (dd, J = 12.6, 7.9 Hz, 2H), 3.72 (s, 3H), 3.63 (dt, J = 21.4, 9.8 Hz, 2H), 3.55 – 3.49 (m, 2H), 3.37 (s, 3H).

## Synthesis of 1-methyl-3-(2-(2-(2-methoxyethoxy)-ethoxy)ethyl) imidazolium bis(trifluoromethyl-sulfonyl)amide

1-methylimidazole (99 % pure, 67 mL, 416.6 mmol) and methanesulfonic acid 2-(2-(2-methoxyethoxy)ethoxy)ethyl ester (96.1 g, 396.6 mmol) were mixed under an inert atmosphere and heated to 60 °C for 1 day before cooled to RT. The reaction mixture was dissolved in dichloromethane (400 mL) before $LiNTf_2$ (99 % pure, 114.64 g, 395.4 mmol), dissolved in demineralized $H_2O$ (400 mL), was slowly added. The reaction mixture was stirred for 72 hours before extracting with dichloromethane. The solvent was removed *in vacuo*.

Yield: > 99 %

$^1$H NMR (600 MHz, $CDCl_3$): δ 8.82 (s, 1H), 7.47 (s, 1H), 7.25 (t, J = 1.8 Hz, 1H), 4.37 – 4.32 (m, 2H), 3.93 (d, J = 4.7 Hz, 2H), 3.85 – 3.81 (m, 2H), 3.68 – 3.64 (m, 2H), 3.62 (dt, J = 6.5, 3.5 Hz, 4H), 3.57 – 3.54 (m, 2H), 3.36 (s, 3H).

## Synthesis of 1-*H*-3-(2-(2-methoxyethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)amide

HCl(aq) (37 % pure, 55 mL, 669.8 mmol) was added dropwise to a solution of 1-(2-(2-methoxyethoxy)ethyl) imidazole (75.3 g, 442.4 mmol) in ethanol (200 mL), while cooling the mixture in an ice bath. The reaction mixture was stirred for 30 minutes before removing the ice bath and then additional 3 hours at RT. Excess HCl(aq) and ethanol was removed *in vacuo* and the crude product was dissolved in dichloromethane (400 mL). A solution of $LiNTf_2$ (99 % pure, 136.1 g, 469.3 mmol) in demineralized $H_2O$ (400 mL) was slowly added and the reaction mixture was stirred for 16 hours at RT. The reaction mixture was extracted with dichloromethane before evaporating the solvent off *in vacuo*.

Yield: 169.39 g (85 %)

$^1$H NMR (600 MHz, $CDCl_3$): δ 7.53 (s, 1H), 7.29 (s, 1H), 7.00 (d, J = 10.1 Hz, 1H), 4.12 (t, J = 5.3 Hz, 2H), 3.74 (t, J = 5.3 Hz, 2H), 3.61 – 3.47 (m, 4H), 3.37 (s, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 137.50, 129.18, 119.39, 71.85, 70.65, 70.58, 59.04, 47.02.

## Synthesis of 1-*H*-3-(2-(2-(2-methoxyethoxy)ethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)amide

HCl(aq) (37 % pure, 28 mL, 340.98 mmol) was added dropwise to a solution of 1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl) imidazole (95.68 g, 205.0 mmol) in ethanol (100 mL), while cooling the mixture in an ice bath. The reaction mixture was stirred for 30 minutes before removing the ice bath and then additional 3 hours at RT. Excess HCl(aq) and ethanol was removed *in vacuo* and the crude product was dissolved in dichloromethane (250 mL). A solution of $LiNTf_2$ (99 % pure, 64.33 g, 221.5 mmol), in demineralized $H_2O$ (250 mL), was slowly added and the reaction mixture was stirred for 1 hour at RT. The reaction mixture was extracted with dichloromethane before evaporating the solvent off *in vacuo*.

Yield: 64.53 g (62 %)

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 8.60 (s, 1H), 7.55 – 7.42 (m, 1H), 7.42 (t, J = 1.6 Hz, 1H), 7.30 (t, J = 1.6 Hz, 1H), 4.43 – 4.31 (m, 2H), 3.88 – 3.82 (m, 2H), 3.68 – 3.64 (m, 2H), 3.62 (ddd, J = 6.4, 4.7, 2.0 Hz, 4H), 3.58 – 3.55 (m, 2H), 3.37 (d, J = 3.9 Hz, 3H).

## Synthesis of 1-octyl-3-(2-(2-methoxyethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)amide

1-octyl imidazole (31.09 g, 172.5 mmol) and methanesulfonic acid 2-(2-methoxyethoxy)ethyl ester (34.38 g, 173.4 mmol) were mixed in an inert atmosphere and heated to 100 °C for 16 hours. The reaction mixture was cooled to RT and dissolved in dichloromethane (150 mL) before a solution of $LiNTf_2$ (99 % pure, 53.91 g, 187.78 mmol), in demineralized $H_2O$ (150 mL), slowly was added and the reaction mixture was stirred for 16 hours at RT. The phases were separated before evaporating the solvent *in vacuo*.

Yield: 70.75 g (71 %)

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 8.82 (d, J = 12.7 Hz, 1H), 7.48 (d, J = 27.8 Hz, 1H), 7.28 (dd, J = 19.0, 10.2 Hz, 1H), 4.47 – 4.31 (m, 1H), 4.29 – 4.12 (m, 1H), 3.88 – 3.80 (m, 3H), 3.65 (dd, J = 5.4, 3.3 Hz, 2H), 3.54 (dd, J = 5.4, 3.3 Hz, 2H), 1.93 – 1.79 (m, 2H), 1.38 – 1.14 (m, 10H), 0.88 (t, J = 7.0 Hz, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 135.85, 123.58, 121.64, 120.84, 118.71, 71.53, 70.16, 68.52, 58.88, 50.29, 49.83, 31.63, 29.99, 28.95, 28.82, 26.15, 22.55, 14.01.

## Synthesis of 2-methyl-1,3-bis-(2-(2-methoxyethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)amide

2-methyl imidazole (98 % pure, 4.80 g, 57.3 mmol) was mixed with toluene (450 mL) in an inert atmosphere. Triethylamine (99 % pure, 8.55 g, 83.7 mmol) was added, followed by methanesulfonic acid 2-(2-methoxyethoxy)ethyl ester (22.69 g, 114.5 mmol). The reaction mixture was heated to 90 °C for 16 hours, before cooling to RT and separation of the phases. Dichloromethane (80 mL) was added to the IL phase and $LiNTf_2$ (99 % pure, 20.44 g, 57.2 mmol) dissolved

in demineralized $H_2O$ (80 mL) was added. The reaction mixture was stirred at RT for 2.5 hours before extraction with dichloromethane and removal of the solvent *in vacuo*.

Yield: > 99 %

$^1$H NMR (600 MHz, $CDCl_3$): δ 7.36 (m, 2H), 7.30 – 7.22 (m, 1H), 4.27 (dd, J = 11.3, 6.4 Hz, 4H), 3.85 – 3.79 (m, 4H), 3.63 – 3.51 (m, 4H), 3.51 – 3.44 (m, 4H), 3.33 (m, 6H), 2.64 (d, J = 8.3 Hz, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 121.66, 120.84, 118.69, 71.62, 70.47, 68.84, 48.77, 47.23, 8.59.

## Synthesis of 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-methoxy-ethoxy)ethyl) imidazolium bromide

1-(2-(2-methoxyethoxy)ethyl) imidazole (10.1 g, 59.3 mmol) was dissolved in THF (30 mL) under an inert atmosphere and cooled to 0 °C. Ethyl bromoacete (98 % pure, 12.4 g, 78.8 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 hour and then at RT for 16 hours. THF was then decanted off and the crude product was washed with diethyl ether (2 × 25 mL).

Yield: > 99 %

$^1$H NMR (600 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.68 (s, 1H), 7.62 (d, J = 8.7 Hz, 1H), 5.45 (s, 3H), 4.64 – 4.55 (m, 2H), 4.35 – 4.23 (m, 2H), 3.99 – 3.89 (m, 2H), 3.70 – 3.62 (m, 2H), 3.58 – 3.52 (m, 2H), 3.36 (s, 3H), 1.36 – 1.27 (m, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 166.15, 138.12, 123.26, 122.91, 71.64, 70.39, 68.86, 62.93, 58.95, 50.35, 50.05, 14.09.

## Synthesis of 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-methoxy-ethoxy)ethyl) imidazolium bis(trifluoromethylsulfonyl)-amide

1-(2-ethoxy-2-oxoethyl)-3-(2-(2-methoxyethoxy)ethyl) imidazolium bromide (16.3 g, 48.3 mmol) was dissolved in dichloromethane (40 mL) and $LiNTf_2$ (99 % pure, 20.8 g, 71.7 mmol) dissolved in demineralized $H_2O$ (40 mL) was added. The reaction mixture was stirred at RT for 2 hours before removing the solvent *in vacuo*.

Yield: 17.54 g (67 %)

$^1$H NMR (600 MHz, $CDCl_3$): δ 8.88 (s, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.38 (s, 1H), 5.02 (d, J = 11.6 Hz, 3H), 4.41 – 4.32 (m, 2H), 4.31 – 4.24 (m, 2H), 3.85 (dd, J = 11.7, 7.1 Hz, 2H), 3.67 – 3.61 (m, 2H), 3.58 – 3.49 (m, 2H), 3.36 (s, 3H), 1.38 – 1.26 (m, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 165.72, 137.35, 123.36, 123.07, 120.79, 71.49, 70.29, 68.48, 63.14, 58.85, 50.05, 50.00, 13.82.

## Synthesis of 1-methyl-3-(2-ethoxy-2-oxoethyl) imidazolium bromide

1-methyl imidazole (99.5 % pure, 3.2 mL, 40.15 mmol) was dissolved in THF (20 mL) under an inert atmosphere and cooled to 0 °C. Ethyl bromoacete (98 % pure, 10.1 g, 59.3 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 hour and then at RT for 16 hours. The solvent was decanted off and the crude product was washed with diethyl ether (2 × 15 mL). The product was dried *in vacuo*.

Yield: > 99 %

$^1$H NMR (600 MHz, $CDCl_3$): δ 10.08 (s, 1H), 7.75 (s, 1H), 7.63 (s, 1H), 5.50 (s, 2H), 4.34 – 4.20 (m, 2H), 3.74 (m, 1 h), 4.11 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 166.18, 138.25, 123.98, 123.17, 62.96, 50.36, 36.95, 14.11.

## Synthesis of 1-methyl-3-(2-ethoxy-2-oxoethyl) imidazolium bis(trifluoromethylsulfonyl)amide

1-methyl imidazole (99.5 % pure, 25.5 mL, 318.3 mmol) was dissolved in THF (160 mL) under an inert atmosphere and cooled to 0 °C. Ethyl bromoacete (98 % pure, 70.90 g, 416.0 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 hour and then at RT for 16 hours. The solvent was decanted off and the crude product washed with diethyl ether (2 × 50 mL). Dichloromethane (150 mL) was added and $LiNTf_2$ (99 % pure, 99.3 g, 342.4 mmol) dissolved in demineralized $H_2O$ (150 mL) was added. The reaction mixture was stirred at RT for 2 hours before extraction with dichloromethane and removing the solvent *in vacuo*.

Yield: 146.45 g (99 %)

$^{1}H$ NMR (600 MHz, $CDCl_3$): δ 8.88 (s, 1H), 8.68 (s, 1H), 5.00 (s, 2H), 4.26 – 4.21 (m, 2H), 3.98 (s, 1H), 3.92 (s, 3H), 1.28 (td, J = 7.1, 1.5 Hz, 3H).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ 165.91, 137.23, 123.95, 123.41, 120.80, 63.23, 62.93, 49.82, 36.24, 13.52.

## Synthesis of 1-octyl-3-(2-ethoxy-2-oxoethyl) imidazolium bis(trifluoromethylsulfonyl)amide

1-octyl imidazole (48.60 g, 269.6 mmol) was dissolved in THF (150 mL) under an inert atmosphere and cooled to 0 °C. Ethyl bromoacete (98 % pure, 59.22 g, 349.3 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 hour and then at RT for 16 hours. The solvent was removed *in vacuo* and the crude product washed with diethyl ether (2 × 100 mL). Dichloromethane (150 mL) was added and $LiNTf_2$ (99 % pure, 78.8 g, 271.7 mmol), dissolved in demineralized $H_2O$ (150 mL), was added. The reaction mixture was stirred at RT for 2 hours before extraction with dichloromethane and removal of the solvent *in vacuo*.

Yield: 92.65 g (61 %)

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 8.85 (s, 1H), 7.41 (s, 1H), 7.31 (s, 1H), 5.04 (s, 2H), 4.32 – 4.12 (m, 4H), 1.89 (dd, J = 18.2, 11.4 Hz, 2H), 1.29 (ddd, J = 19.8, 11.5, 6.6 Hz, 13H), 0.87 (t, J = 6.8 Hz, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 165.76, 136.97, 123.97, 121.80, 120.79, 118.66, 63.16, 50.50, 50.02, 31.61, 29.96, 28.91, 28.78, 26.04, 22.55, 14.00, 13.82.

## Synthesis of 2-methyl-1,3-bis- (2-ethoxy-2-oxoethyl) imidazolium bis(trifluoromethylsulfonyl)amide

2-methylimidazole (98 % pure, 37.35 g, 445.0 mmol) was dissolved in toluene (275 mL) and triethylamine (99 % pure, 75 mL, 532.4 mmol) was added. The mixture was cooled to 0 °C before dropwise addition of ethyl bromoacetate (98 % pure, 76.8 g, 450.7 mmol). The reaction mixture was refluxed (100 °C) for 16 hours. A precipitate was discarded and the brown liquid dissolved in dichloromethane (20 mL) and washed with demineralized $H_2O$ (20 mL) before evaporating the solvent *in vacuo*, yielding 27.96 g (37 %) of the intermediate. The intermediate was mixed with THF (80 mL) under an inert atmosphere and cooled to -5 °C. Ethyl bromoacetate (98 % pure, 34.0 g, 199 mmol) was added dropwise. The reaction mixture was stirred at -5 °C for 1 hour and then at RT for 20 hours. The resulting mixture was very viscous and more THF had to be added to transfer the mixture to a round bottomed flask and the solvent was evaporated *in vacuo* giving a white crude product (57.07 g, quantitative). From this, 55.45 g was dissolved in demineralized $H_2O$ (150 mL) and $LiNTf_2$ (99 % pure, 52.8 g, 182.1 mmol) in demineralized $H_2O$ (100 mL) was added. After stirring for 1 hour, dichloromethane (200 mL) was added to the reaction mixture. The phases were separated and the solvent from the organic phase was removed *in vacuo*.

Yield (over three steps): 84.24 g (35 %)

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 7.31 (d, J = 6.2 Hz, 2H), 7.29 – 7.24 (m, 1H), 4.96 (s, 4H), 4.28 (m, 4H), 2.53 (d, J = 6.2 Hz, 3H), 1.34 – 1.29 (m, 6H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 165.39, 146.63, 122.43, 63.24, 49.30, 13.84, 10.11.

## Synthesis of (2-(2-methoxyethoxy)ethyl)trioctyl phosphonium mesylate

Trioctylphosphine (97 % pure, 32.0 mL, 69.5 mmol) was stirred under an inert atmosphere and mesyalate 2-(2-methoxyethocy)ethyl) ester (14.0 g, 70.6 mmol) was slowly added. The reaction mixture was heated to 90 °C for 20 hours. The crude product was dried *in vacuo* overnight.

Yield: 34.30 g (87 %)

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 3.90 (dt, J = 20.0, 5.8 Hz, 2H), 3.63 – 3.58 (m, 2H), 3.49 (dt, J = 14.4, 6.9 Hz, 2H), 3.35 (s, 3H), 3.10 (d, J = 4.0 Hz, 1H), 2.89 – 2.80 (m, 2H), 2.77 (s, 3H), 2.35 – 2.24 (m, 6H), 1.60 – 1.42 (m, 13H), 1.36 – 1.19 (m, 28H), 0.88 (t, J = 6.9 Hz, 10H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 71.33, 70.11, 58.79, 39.50, 31.70, 30.92, 30.82, 29.01, 28.94, 22.61, 21.83, 19.69, 19.38, 14.12.

$^{31}$P NMR (243 MHz, $CDCl_3$): δ 33.21.

## Synthesis of (2-(2-methoxyethoxy)ethyl)trioctyl phosphonium bis(trifluoromethylsulfonyl)amide

(2-(2-methoxyethoxy)ethyl)trioctylphosphonium mesylate (24.53 g, 43.1 mmol) was dissolved in demineralized $H_2O$ (75 mL) and $LiNTf_2$ (99 % pure, 16.3 g, 56.2 mmol) in demineralized $H_2O$ (75 mL) was added. After stirring for 16 hours the phases were separated and the crude product was dried *in vacuo* over night.

Yield: 28.47 g (88 %)

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 3.88 – 3.79 (m, 1H), 3.64 – 3.48 (m, 3H), 3.35 (s, 2H), 2.54 (dt, J = 11.8, 5.9 Hz, 1H), 2.20 – 2.08 (m, 5H), 1.57 – 1.40 (m, 11H), 1.36 – 1.19 (m, 24H), 0.88 (t, J = 6.9 Hz, 9H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 71.24, 70.29, 58.79, 31.78, 31.65, 30.73, 30.62, 29.08, 28.95, 28.75, 22.64, 22.59, 21.56, 21.53, 19.56, 19.25, 14.14, 14.10.

$^{31}$P NMR (243 MHz, $CDCl_3$): δ 33.45.

## Synthesis of (2-ethoxy-2-oxoethyl)trioctylphosphonium bromide

Trioctylphosphine (97 % pure, 27.5 mL, 59.7 mmol) in THF (40 mL) was cooled to 0 °C under an inert atmosphere. Ethyl bromoacetate (98 % pure, 15.5 g, 90.9 mmol) was slowly added. After stirring at 0 °C for 1 hour, the reaction mixture was refluxed (60 °C) for 16 hours. The solvent was then removed *in vacuo*.

Yield: > 99 %

$^{1}$H NMR (600 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.03 (d, J = 24.8 Hz, 1H), 6.90 (s, 1H), 4.09 (t, J = 5.2 Hz, 2H), 3.69 (t, J = 5.2 Hz, 2H), 3.54 (dd, J = 10.4, 6.4 Hz, 2H), 3.47 – 3.41 (m, 2H), 3.28 (d, J = 8.0 Hz, 3H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 62.91, 31.65, 30.77, 30.66, 28.94, 28.88, 22.59, 21.90, 21.87, 19.71, 19.39, 14.11, 13.97.

$^{31}$P NMR (243 MHz, $CDCl_3$): δ 31.91.

## Synthesis of 2-ethoxy-2-oxoethyl)trioctylphosphonium bis(trifluoromethylsulfonyl)amide

(2-ethoxy-2-oxoethyl)trioctylphosphonium bromide (24.87 g, 46.3 mmol) was suspended in demineralized $H_2O$ (75 mL) and $LiNTf_2$ (99 % pure, 14.2 g, 49.0 mmol) in demineralized $H_2O$ (75 mL) was added. After stirring for 16 hours the phases were separated and the crude product was dried *in vacuo* overnight.

Yield: 28.01 g (82 %)

$^{1}$H NMR (600 MHz, $CDCl_3$) δ 4.25 (q, J = 7.2 Hz, 2H), 3.47 (d, J = 12.9 Hz, 2H), 2.31 – 2.19 (m, 6H), 1.59 – 1.41 (m, 12H), 1.38 – 1.21 (m, 28H), 0.88 (t, J = 6.9 Hz, 9H).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 63.23, 31.61, 30.55, 30.44, 28.88, 28.68, 22.57, 21.50, 21.47, 19.21, 18.90, 14.09, 13.84.

$^{31}$P NMR (243 MHz, $CDCl_3$): δ 32.27.

## Synthesis of (1-butyl-3-methyl imidazolium)$_3$PW$_{12}$O$_{40}$

$H_3PW_{12}O_{40}$ (26.26 g, 9.1 mmol) was dissolved in demineralized $H_2O$ (350 mL) and 1-butyl-1-methyl imidazolium chloride (5.1 g, 29.2 mmol), dissolved in demineralized $H_2O$ (350 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on a glass filter funnel and washed with $H_2O$ (3 × 250 mL). The crude product was dissolved in acetone and concentrated *in vacuo*.

Yield: 24.67 g (82 %)

## Synthesis of (1-(2-ethoxy-2-oxoethyl)-3-(2-(2-methoxyethoxy)ethyl) imidazolium)$_3$PW$_{12}$O$_{40}$

$H_3PW_{12}O_{40}$ (3.14 g, 1.09 mmol) was dissolved in demineralized $H_2O$ (50 mL) and 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-methoxyethoxy)ethyl) imidazolium bromide (1.11 g, 3.0 mmol), dissolved in demineralized $H_2O$ (50 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on a glass filter funnel and washed with $H_2O$ (3 × 30 mL). The crude product was dissolved in acetone and concentrated *in vacuo*.

Yield: 3.34 g (84 %)

## Synthesis of (1-methyl-3-(2-ethoxy-2-oxoethyl) imidazolium)$_3$PW$_{12}$O$_{40}$

$H_3PW_{12}O_{40}$ (3.84 g, 1.33 mmol) was dissolved in demineralized $H_2O$ (50 mL) and 1-methyl-3-(2-ethoxy-2-oxoethyl) imidazolium bromide (1.08 g, 4.4 mmol), dissolved in demineralized $H_2O$ (50 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on

a glass filter funnel and washed with $H_2O$ (3 × 30 mL). The crude product was dissolved in acetone and concentrated *in vacuo*.

Yield: 3.88 g (87 %)

## Synthesis of (1,2-dimethyl-3-propyl imidazolium)$_3PW_{12}O_{40}$

$H_3PW_{12}O_{40}$ (4.37 g, 1.52 mmol) was dissolved in demineralized $H_2O$ (60 mL) and 1,2-dimethyl-3-propyl imidazolium bromide (1.21 g, 5.53 mmol), dissolved in demineralized $H_2O$ (60 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on a glass filter funnel and washed with $H_2O$ (3 × 30 mL). The crude product was dissolved in acetone and concentrated *in vacuo*.

Yield: 3.27 g (67 %)

## Synthesis of (1-butyl-2,3-dimethyl imidazolium)$_3PW_{12}O_{40}$

$H_3PW_{12}O_{40}$ (3.90 g, 1.36 mmol) was dissolved in demineralized $H_2O$ (60 mL) and 1,2-dimethyl-3-butyl imidazolium bromide (1.20 g, 5.15 mmol), dissolved in demineralized $H_2O$ (60 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on a glass filter funnel and washed with $H_2O$ (3 × 30 mL). The crude product was dissolved in acetone and concentrated *in vacuo*.

Yield: 1.50 g (33 %)

## Synthesis of (1-methyl-1-propylpiperidinium)$_3PW_{12}O_{40}$

$H_3PW_{12}O_{40}$ (4.31 g, 1.5 mmol) was dissolved in demineralized $H_2O$ (60 mL) and 1-methyl-1-propylpiperidinium bromide (1.21 g, 5.42 mmol), dissolved in demineralized $H_2O$ (60 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on a glass filter funnel and washed with $H_2O$ (3 × 30 mL). The crude product was dissolved in acetone and concentrated *in vacuo*.

Yield: 3.20 g (65 %)

## Synthesis of (trihexyltetradecylphosphonium)$_3$PW$_{12}$O$_{40}$

$H_3PW_{12}O_{40}$ (2.71 g, 0.9 mmol) was dissolved in demineralized $H_2O$ (40 mL) and trihexyltetradecylphosphonium bromide (1.59 g, 3.1 mmol), dissolved in demineralized $H_2O$ (40 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on a glass filter funnel and washed with $H_2O$ (3 × 30 mL). The crude product was dried *in vacuo*.

Yield: 2.90 g (73 %)

## Synthesis of (triethylsufonium)$_3$PW$_{12}$O$_{40}$

$H_3PW_{12}O_{40}$ (3.56 g, 1.24 mmol) was dissolved in demineralized $H_2O$ (50 mL) and triethylsulfonium iodide (0.99 g, 4.0 mmol), dissolved in demineralized $H_2O$ (50 mL), was added. A white precipitate was instantly formed. After stirring for 10 minutes, the precipitate was collected on a glass filter funnel and washed with $H_2O$ (3 × 30 mL). The crude product was dissolved in acetone and concentrated *in vacuo*.

Yield: 2.87 g (72 %)

## Synthesis of the Iron(III) complex

Kojic acid (25.57 g, 180.1 mmol) and freshly destilled $SOCl_2$ (100 mL) were mixed under an inert atmosphere for 2 hours. The formed yellow precipitate was collected by filtration and washed with hexane. This product was then suspended in anhydrous acetonitrile (500 mL) under an inert atmosphere and *N*-methylimidazole (16.0 mL, 200.7 mmol) was added. The reaction mixture was heated to reflux (85 °C) for 22 hours. The formed precipitate was collected by filtration and washed with ethyl acetate. The crude product was evaporated to dryness *in vacuo* yielding 23.26 (53 %) of the methyl substituted intermediate.

The methyl substituted intermediate (20.01 g, 80.1 mmol) was suspended in anhydrous methanol (200 mL) under an inert atmosphere. $FeCl_3$ (4.41 g, 26.4

mmol) was added and the reaction mixture was heated to reflux (65 °C) for 18 hours. The solvent was removed *in vacuo* yielding the iron(III) complex.

Yield: > 99 %

## Miscibility testing of ILs

The miscibility testing was performed on four different substrates: GMO, EGMS, MHGMS and SNS. All of the substrates were liquid when tested, i.e. GMO, EGMS and MHGMS were melted at 60 °C before testing. SNS is liquid at RT. All ILs were tested in a 1:1 volume ratio with the four substrates. The IL and substrate was thoroughly mixed and checked if one or two phases were formed. If only one phase was formed, the mixture was put into a centrifuge, to see if this could separate the IL and substrate. If still one phase, the mixture was left over night at elevated temperatures. If this still gives one phase, the IL was evaluated as miscible with the IL.

## Initial testing of different catalysts and ILs in the epoxidation with $H_2O_2$

Reaction conditions for the testing were as follows. The IL (3 mL) and catalyst (0.003 equivalents) were mixed and heated to 60 °C. The hydrogen peroxide (1.1 equivalents) was then added, followed by the substrate (either DAGMO (1.1 mL) or GMO (0.9 mL)). Samples were taken after 1 hour, 3 hours and 20 hours. Even if the substrate and product was immiscible with the IL, all of the samples were treated equally. Sample was extracted with heptane, evaporated and silylated before GC analysis.

## Initial testing of epoxidation with peracetic acid

Reactions were performed by mixing substrate (9 mL GMO or 11 mL DAGMO), solvent ([BMIm][$Tf_2N$] or acetic acid, 30 mL) and catalyst ($[BMIm]_3PW_{12}O_{40}$, iron(III) complex). The mixture was heated to 60 °C and adding peracetic acid (5 mL, 1.1 eq) at once. Samples were taken after 3 hours, 5 hours and 24 hours.

Reactions were performed by mixing substrate (9 mL GMO or 11 mL DAGMO), solvent ([BMIm][$Tf_2N$] or acetic acid, 30 mL) and catalyst ($[BMIm]_3PW_{12}O_{40}$, iron(III) complex or no catalyst) . The mixture was heated to 60 °C and adding peracetic acid (5 mL, 1.1 eq) at once. Samples were taken after 15 minutes, 30 minutes, 1 hour and 3 hours.

Reactions were performed by mixing substrate (9 mL GMO or 11 mL DAGMO), acetic acid (30 mL) and acetic anhydride (4.3 mL). The mixture was heated 60 °C and adding peracetic acid (5 mL, 1.1 eq) at once. Samples were taken after 15 minutes, 30 minutes, 1 hour and 3 hours.

Reactions were performed by mixing substrate (9 mL GMO or 11 mL DAGMO) and acetic acid (30 mL). The mixture was heated 30 °C and adding peracetic acid (5 mL, 1.1 eq) at once. Samples were taken after 15 minutes, 30 minutes, 1 hour and 3 hours.

Reactions were performed by mixing GMO (9 mL) and acetic acid (30 mL, 15 mL or 7.5 mL). The mixture was heated 30 °C and adding peracetic acid (5 mL, 1.1 eq) at once. Samples were taken after 15 minutes, 30 minutes, 1 hour and 3 hours.

Reaction was performed by mixing GMO (45 mL) and acetic acid (150 mL). The mixture was heated 30 °C and adding peracetic acid (25 mL, 1.1 eq) over three minutes. Samples were taken after 15 minutes, 30 minutes, 1 hour and 3 hours.

## Optimization of the temperature in epoxidation with peracetic acid

The following experiments were an 11 times up scaling of the original experiments, that is with 99 mL GMO as the substrate. The experiments were performed in a jacketed reaction vessel, compared to the small scale experiments in round-bottomed flasks. Stirring was done with a Teflon stirrer at 200 RPM.

A reaction was performed by mixing GMO (99 mL) and acetic acid (330 mL). The mixture was cooled to 10 °C or 20 °C or heated 30 °C or 40 °C and adding

peracetic acid (55 mL, 1.1 eq) over 20-25 minutes. Samples were taken after, 30 minutes, 1 hour, 1.5 hours and 2 hours.

Reaction was performed by mixing GMO (99 mL) and acetic acid (990 mL). The mixture was cooled to 20 °C or heated 25 °C or 30 °C and adding peracetic acid (55 mL, 1.1 eq) with 2.5 mL/minute. Samples were taken after 30 minutes, 1 hour, 1.5 hours and 2 hours.

## Optimization of the amount of peracetic acid in epoxidation with peracetic acid

Reaction was performed by mixing GMO (99 mL) and acetic acid (330 mL). The mixture was heated 30 °C and adding peracetic acid (1.01 eq, 1.1 eq, and 1.5 equivalents) with 2.5 mL/minute. Samples were taken after 30 minutes, 1 hour, 1.5 hours and 2 hours.

## Optimization of the rate of addition of peracetic acid in epoxidation with peracetic acid

Reaction was performed by mixing GMO (99 mL) and acetic acid (330 mL). The mixture was heated 30 °C and adding peracetic acid (1.1 eq. or 1.5 eq.) with 2.5 mL/minute or 5 mL/minute. Samples were taken after 30 minutes, 1 hour, 1.5 hours and 2 hours.

## Epoxidation with peracetic acid in larger scale

Reaction was performed by mixing GMO (180 mL) and acetic acid (1.8 L). The mixture was heated 25 °C and adding peracetic acid (1.1 eq., 1.5 eq., 2 eq. or 5 equivalents) over approximately 23 minutes. Samples were taken in the interval 30 minutes to 4.5 hours.

## Catalytic transfer hydrogenation of modelsubstrates

Three different model substrates were tested in the reduction using a hydrogen donor: cyclooctene oxide, cyclohexene oxide and methyl cinnamate. Three different hydrogen donors were tested: $NH_4HCO_2$ (3 equivalents) 2-propanol (1.8 equivalents, with either HCl(aq) or KOH (0.1 equivalents) as co-catalyst) and a mixture of formic acid and triethylamine ($Et_3N$) in the ratio 5:2 or 1:1 (HCOOH:$Et_3N$ 5:2 or 1:1) (2 equivalents of HCOOH). Three different catalysts have been tested: $Pd(OAc)_2$ (added in 0.1 equivalents), Pd/C (added in 0.05 equivalents) and Ru/C (added in 0.1 equivalents).

Solvents tested: [BMIm][$BF_4$], [BMIm][$Tf_2N$], [EMIm][$Tf_2N$], [EMIm][$EtOSO_3$], [$C_5O_2OcIm$][$Tf_2N$], [BMIm][Cl], [$P_{6,6,6,14}$][$Tf_2N$], methanol, ethanol, acetic acid, [BMIm][ $BF_4$] : methanol 1:1, [BMIm][ $Tf_2N$] : methanol 1:1, or neat. The amount of solvent was 1 L, 1.5 mL or 2 mL to 0.5 mmol substrate.

Reactions have been performed different temperatures (RT, 30 °C, 45 °C, 50 °C, 60 °C, 65 °C, 80 °C) for 1 day or 3 days.

Workup of the reaction mixture before analysis (either NMR or GC): for ILs: extraction with heptane followed by filtration and extraction; for organic solvent: filtration followed by extraction.

## Catalytic transfer hydrogenation of EGMS and EDAGMS

Three different hydrogen donors were tested: $NH_4HCO_2$ (3 equivalents) 2-propanol (1.8 equivalents, with either HCl(aq) or KOH (0.1 equivalents) as co-catalyst) and a mixture of formic acid and triethylamine ($Et_3N$) in the ratio 5:2 or 1:1 (HCOOH:$Et_3N$ 5:2 or 1:1) (2 equivalents of HCOOH). Three different catalysts have been tested: $Pd(OAc)_2$ (0.1 equivalents), Pd/C (0.05 equivalents) and Ru/C (0.1 equivalents).

Solvents tested: [BMIm][$Tf_2N$], [$P_{6,6,6,14}$][$Tf_2N$], acetic acid. The amount of solvent was 2 mL to 0.5 mmol substrate.

Reactions have been performed different temperatures (RT, 30 °C, 45 °C, , 60 °C, , 80 °C) for 1 hour, 4 hours or 1 day.

Workup of the reaction mixture before analysis by GC: for ILs: extraction with heptane followed by filtration and extraction; for organic solvent: filtration followed by extraction.

## Hydrogenation with molecular $H_2$

The epoxide for the reaction was synthesized as follows. GMO and acetic acid were mixed in a 1:10 ratio, heated to 25 °C before peracetic acid (1.5 equivalents) was added over 23 minutes. The total reaction time was three hours, after which the reaction mixture was transferred to the autoclave without further work-up. Samples were taken after three hours to be sure the substrate for hydrogenation was EGMS.

Three different autoclaves were tested, two small ones and a slightly larger one. The small one could contain approximately 20 g or 100 g of reaction mixture and hydrogenations were performed with a stirring speed of 600 RPM. The larger one could contain approximately 1500 g of reaction mixture and stirring was 900 RPM. Unless it was specified, reactions were performed at RT.

When Pd/C was used as a catalyst, a small amount was added, and after the gas formation stopped, the rest of the catalyst was added.

5 g Pd/C (10 %) was added to 1500 g reaction mixture. 5 bar $H_2$(g) was applied. Samples were taken after 10 minutes, 1.5 hours and 2.5 hours.

5 g Pd/C (10 %) was added to 1500 g reaction mixture. 2 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 45 minutes, 1 hour, 1.5 hours and 2 hours.

0.5 g Pd/C (10 %) was added to 1500 g reaction mixture. 2 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 45 minutes, 1 hour, 1.5 hours and 2 hours. 5 bar $H_2$(g) was then applied. Sampes were taken after 15 minutes, 30 minutes and 45 minutes.

2 g Pd/C (10 %) was added to 1500 g reaction mixture. 2 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours. This

experiment was also tested in the small autoclave with same reaction conditions (0.15 g Pd/C to 100 mL reaction mixture).

4 g Pd/C (10 %) was added to 1500 g reaction mixture. 3 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours. This experiment was also tested in the small autoclave with same reaction conditions (0.3 g Pd/C to 100 mL reaction mixture).

4 g Pd/C (10 %) was added to 1500 g reaction mixture. 10 bar $H_2$(g) or 15 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours.

0.5 g Pd/C (10 %) was added to 20 g reaction mixture. 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours.

3 g $MnO_2$ was added to 1500 g reaction mixture. After the gas formation had stopped, the reaction mixture was filtered and transferred to an autoclave. 4 g Pd/C (10 %) was added and 10 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 1 hour, and 2 hours.

Experiments with lower amount of peracetic acid from the epoxidation were performed as follows: 4 g Pd/C (10 %) was added and 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 1 hour, and 2 hours. The amount of peracetic acid used in these experiments were 1.01 equivalents and 0.9 equivalents.

Experiments with acetaldehyde reaction after the epoxidation reaction, were as follows: 4 g Pd/C (10 %) was added and 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 1 hour, and 2 hours. The amount of acetaldehyde used in these experiments was 20 mL.

Experiment with ultrasound treatment was performed as follows: 4 g Pd/C (10 %) was added and 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 1 hour, and 2 hours. Ultrasound treatment was performed at 4 × 10 minutes.

20 g Pricat9910 (from Johnson Matthey) was added to 1500 g reaction mixture. 20 bar $H_2$(g) was applied. A sample was taken after 11 hours.

Raney Nickel was added to 1500 g reaction mixture. 20bar $H_2$(g) was applied and the reaction mixture was heated to 40 °C. Samples were taken after 2 hours and 17 hours.

2 g Pt/C (10 %) was added to 1500 g reaction mixture. 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours.

4 g Pd/$BaSO_4$ (5 %) was added to 1500 g reaction mixture. 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours.

2 g Pd/C (10 %) was added to 1500 g reaction mixture containing $BaSO_4$ (3 g). 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours.

1 g Rh/C (5 %) was added to 100 g reaction mixture and ultrasound treatment was applied before hydrogenation was started. 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours.

1 g Ru/C (5 %) was added to 100 g reaction mixture. 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 30 minutes, 1 hour, and 2 hours.

For the epoxidation and hydrogenation of DHGMS: 220 mL DAGMO in 1.8 L acetic acid was heated to 25 °C and peracetic acid (137 mL, 1.5 mL) was added over 23 minutes. After 3 hours the reaction mixture was transferred to an autoclave. 2 g Pd/C (10 %) was added to 1500 g of the reaction mixture. 5 bar $H_2$(g) was applied. Samples were taken after 15 minutes, 1 hour, and 2 hours.

For the epoxidation and hydrogenation of oleic acid: Peracetic acid (75 mL) was cooled to 0 °C and oleic acid (92 mL) was added over 1.5 hour. The reaction mixture was heated to 25 °C and stirred for 3.5 hours. The reaction mixture was poured into icecold demineralized water followed by decantation of the aqueous phase. The crude product was dispensed in hexane, filtered and evaporated to dryness *in vacuo*. This product (30 g) was dissolved in acetic acid (60 mL) and Pd/C (3 g) was added. 3 bar $H_2$(g) was applied. Samples were taken after 1 hour, 2 hours and 5 hours. Work-up method for the samples was different from the workup of the monoglycerides: samples were filtered and demineralized water was added before extraction with diethyl ether.